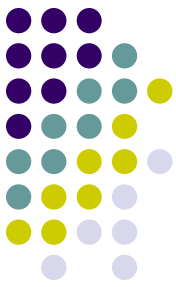


# Lens Metabolism

*What is the primary substrate in lens metabolism?*

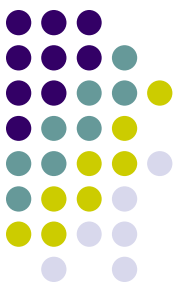
**?**



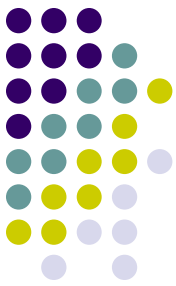
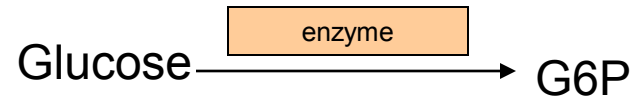
# Lens Metabolism

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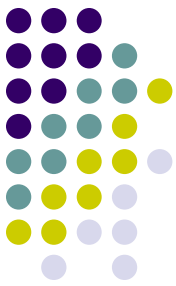
Glucose

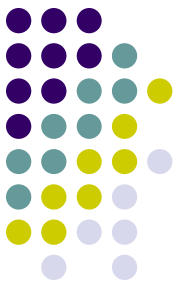


# Lens Metabolism

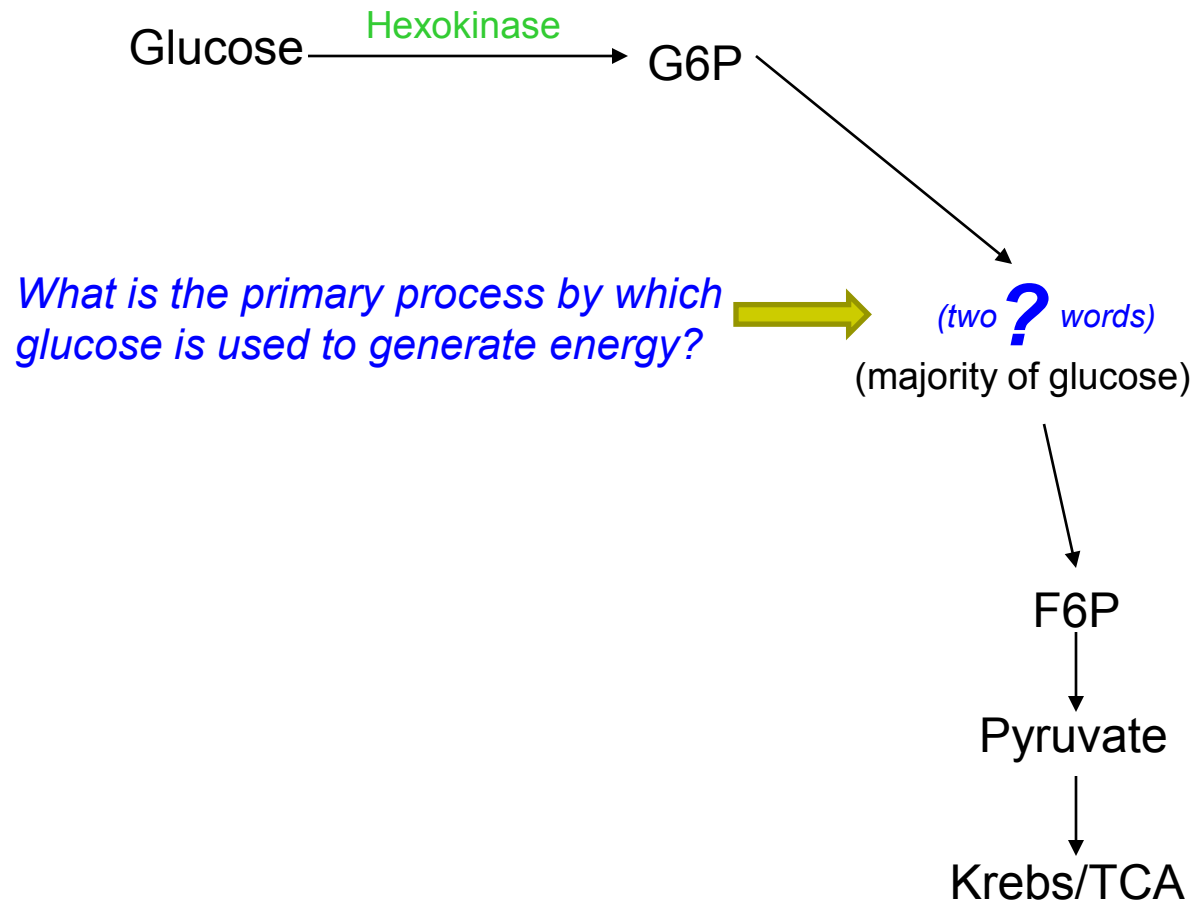


# Lens Metabolism

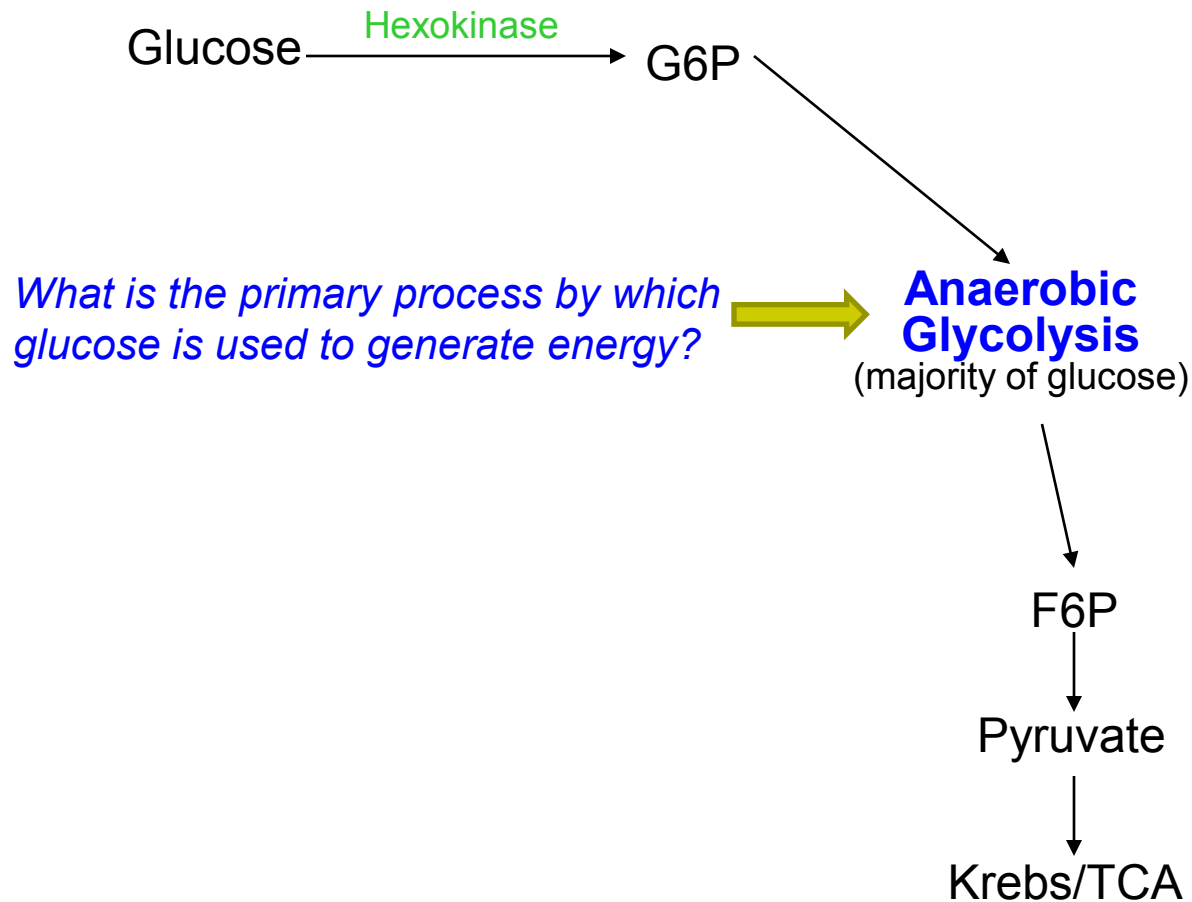
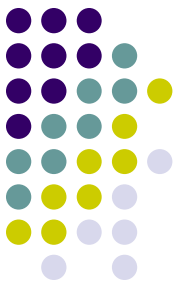




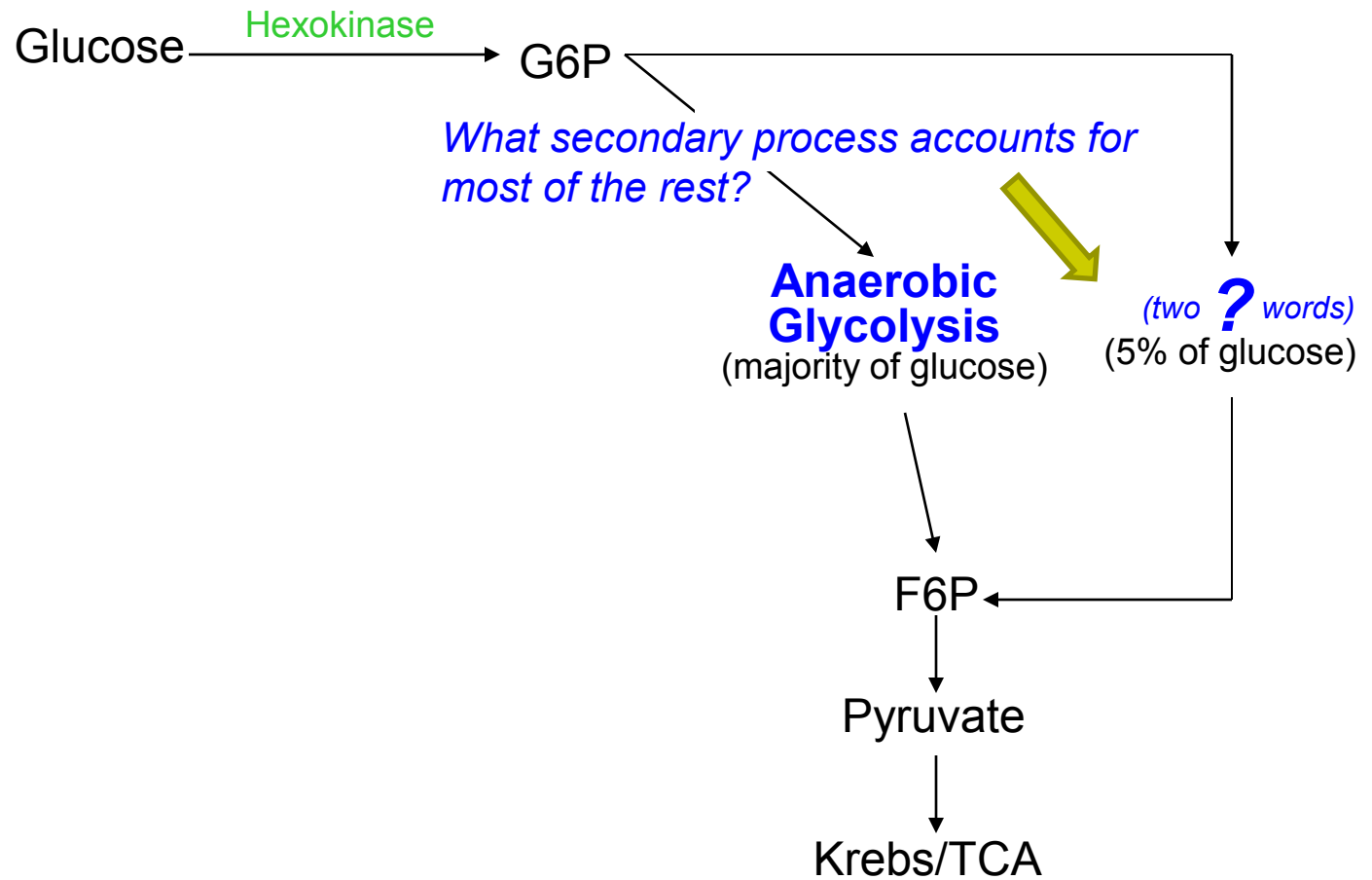
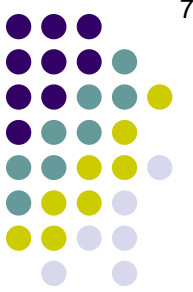
## Lens Metabolism



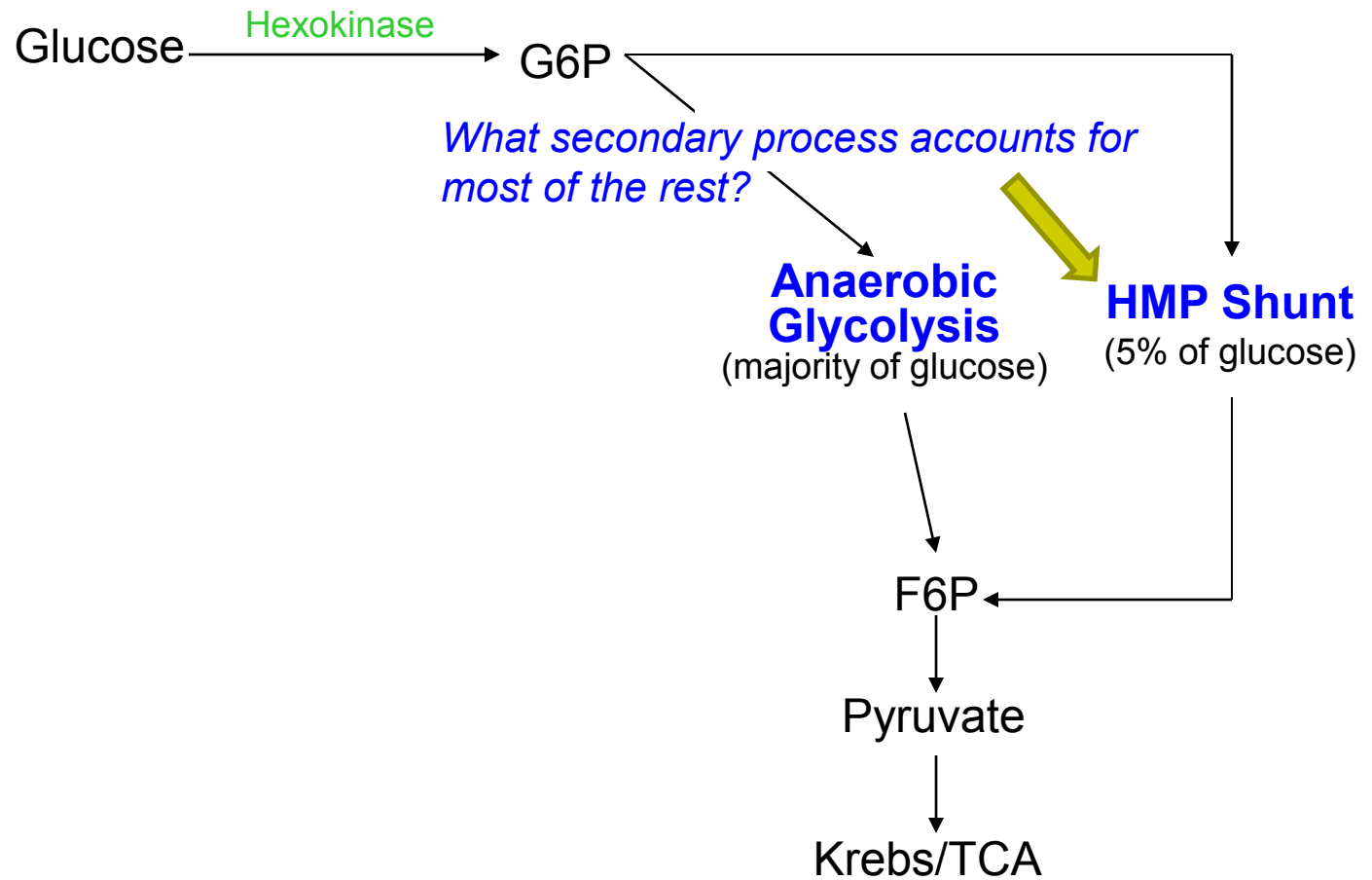
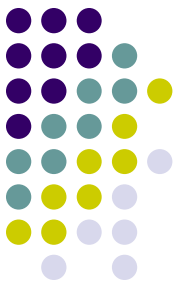
# Lens Metabolism



# Lens Metabolism



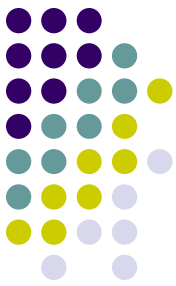
# Lens Metabolism





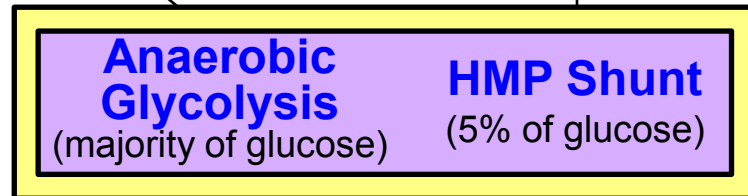
# Lens Metabolism

9



Glucose  $\xrightarrow{\text{Hexokinase}}$  G6P

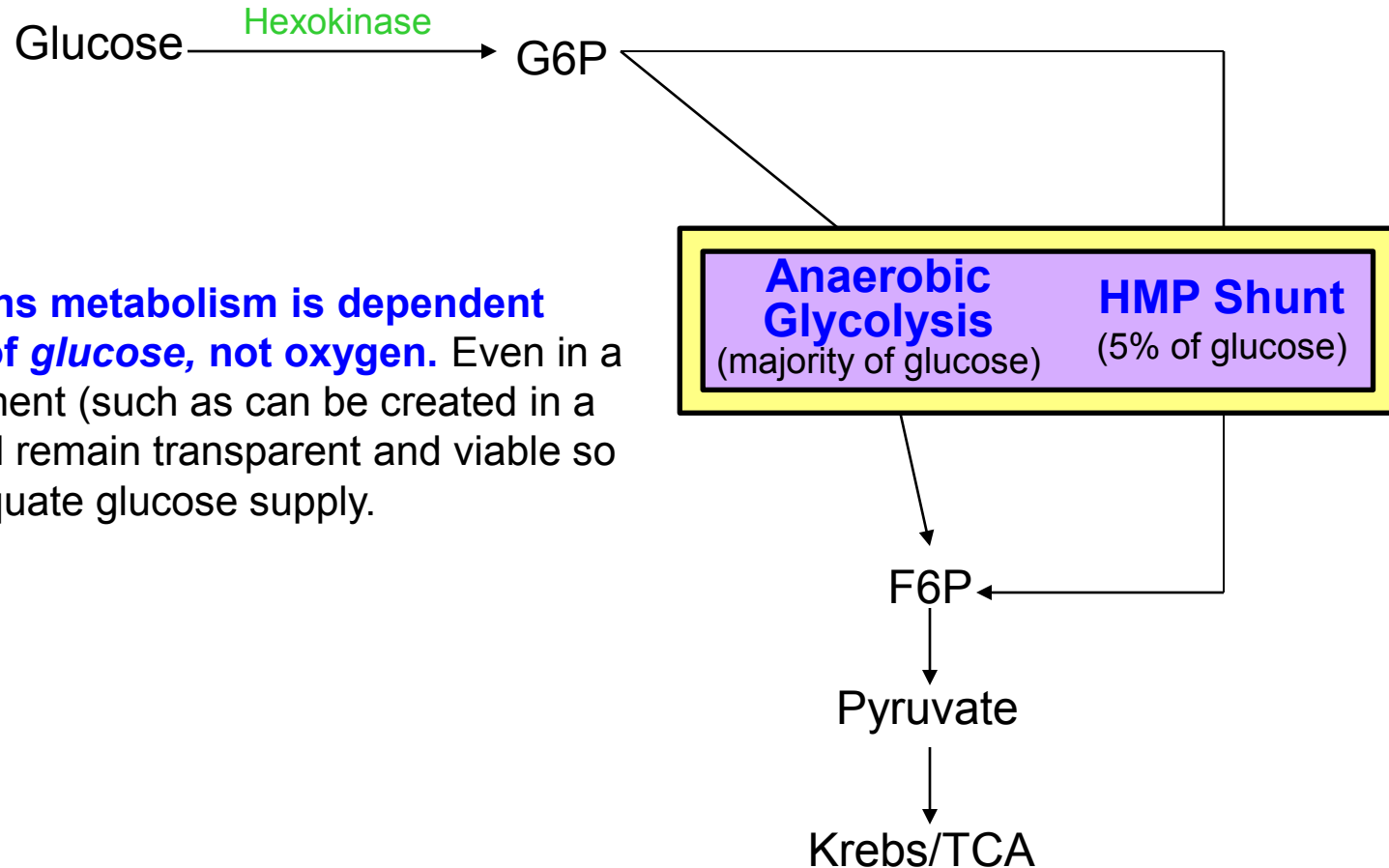
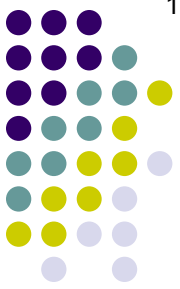
The top-line point: **Lens metabolism is dependent upon the presence of *glucose*, not oxygen.**



F6P  
↓  
Pyruvate  
↓  
Krebs/TCA

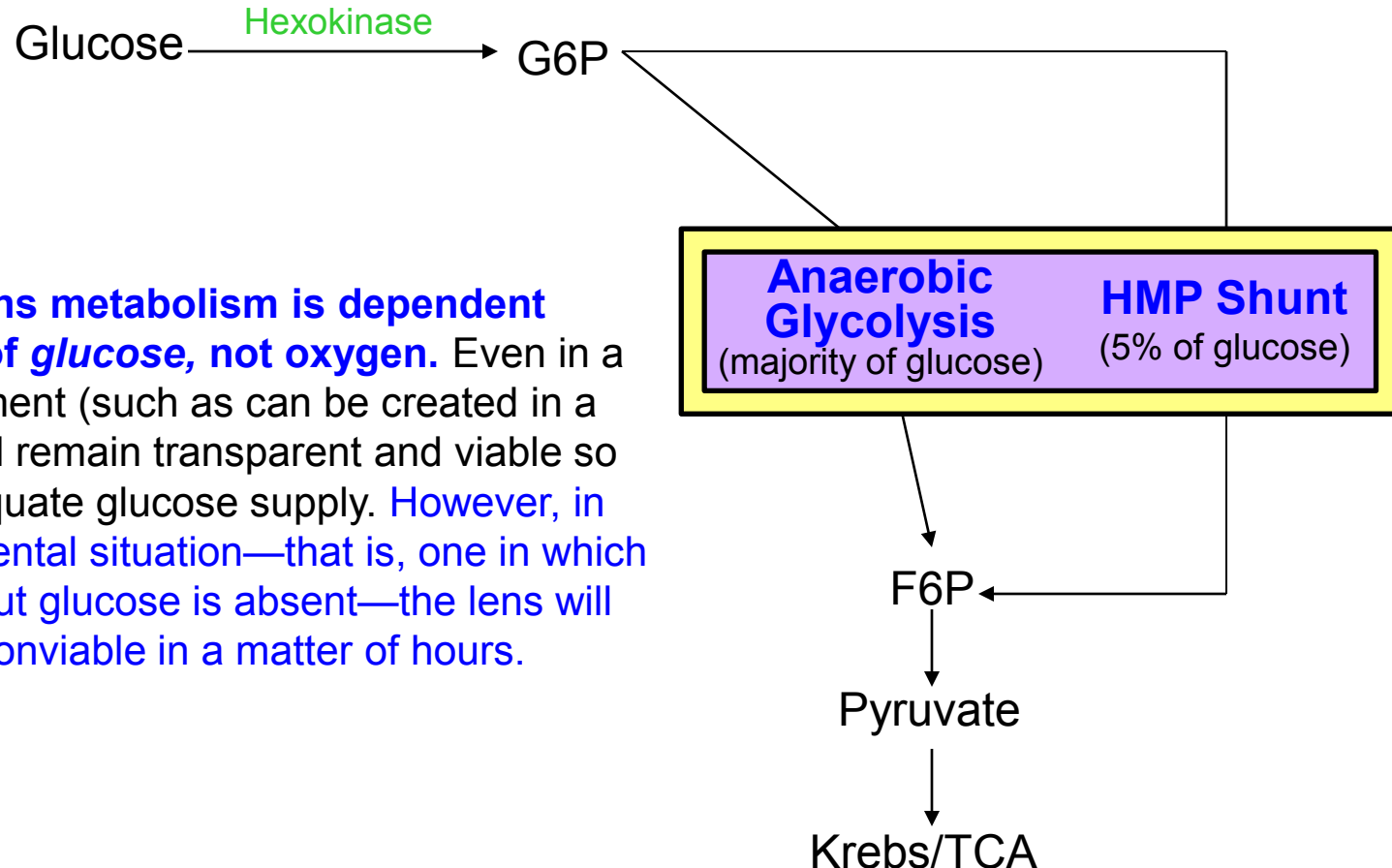
*No question yet—proceed when ready*

# Lens Metabolism



The top-line point: **Lens metabolism is dependent upon the presence of *glucose*, not oxygen.** Even in a zero-oxygen environment (such as can be created in a lab setting), a lens will remain transparent and viable so long as it has an adequate glucose supply.

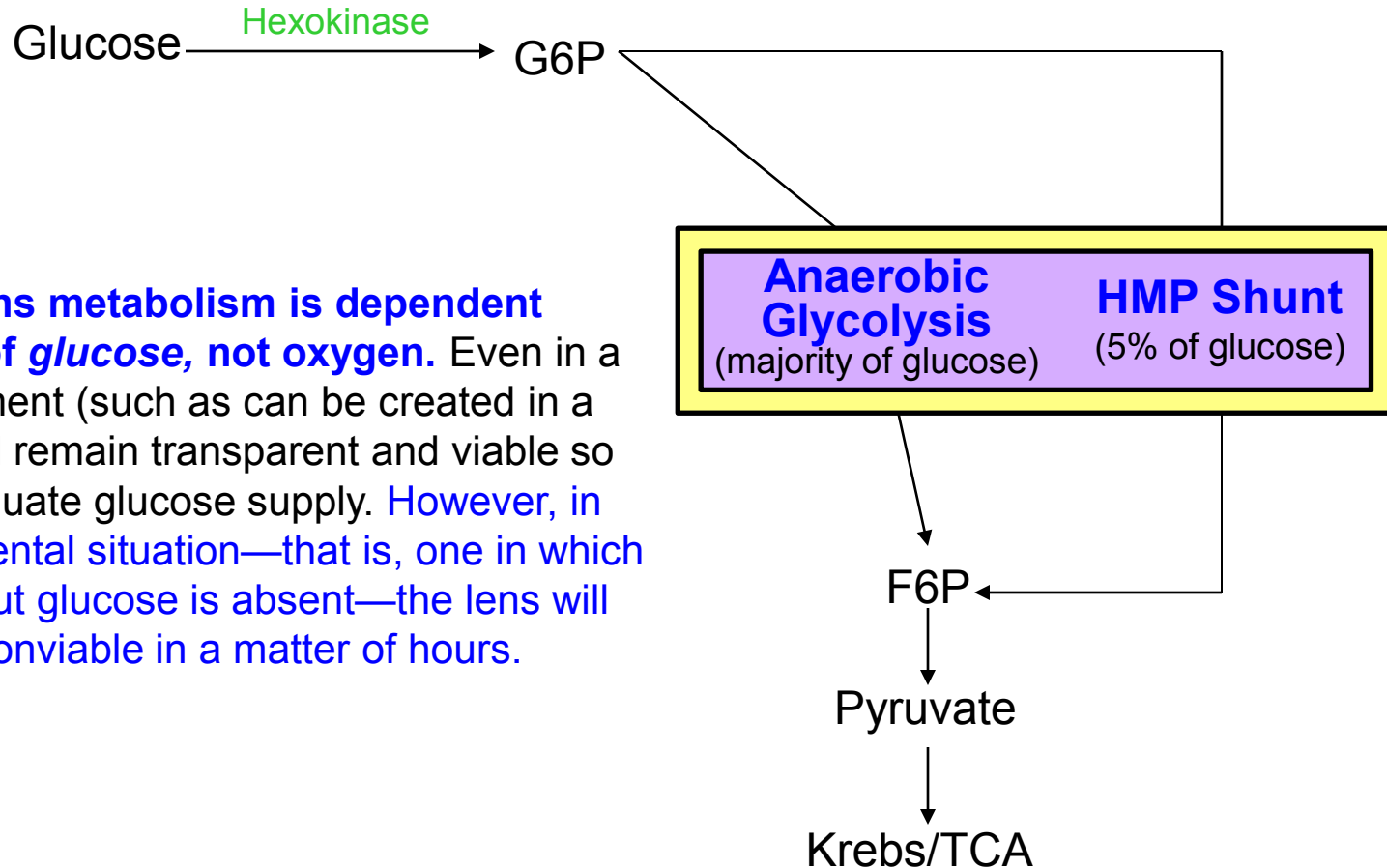
# Lens Metabolism



The top-line point: **Lens metabolism is dependent upon the presence of *glucose*, not *oxygen*.** Even in a zero-oxygen environment (such as can be created in a lab setting), a lens will remain transparent and viable so long as it has an adequate glucose supply. **However, in the reverse environmental situation—that is, one in which oxygen is abundant but glucose is absent—the lens will become cloudy and nonviable in a matter of hours.**

# Lens Metabolism

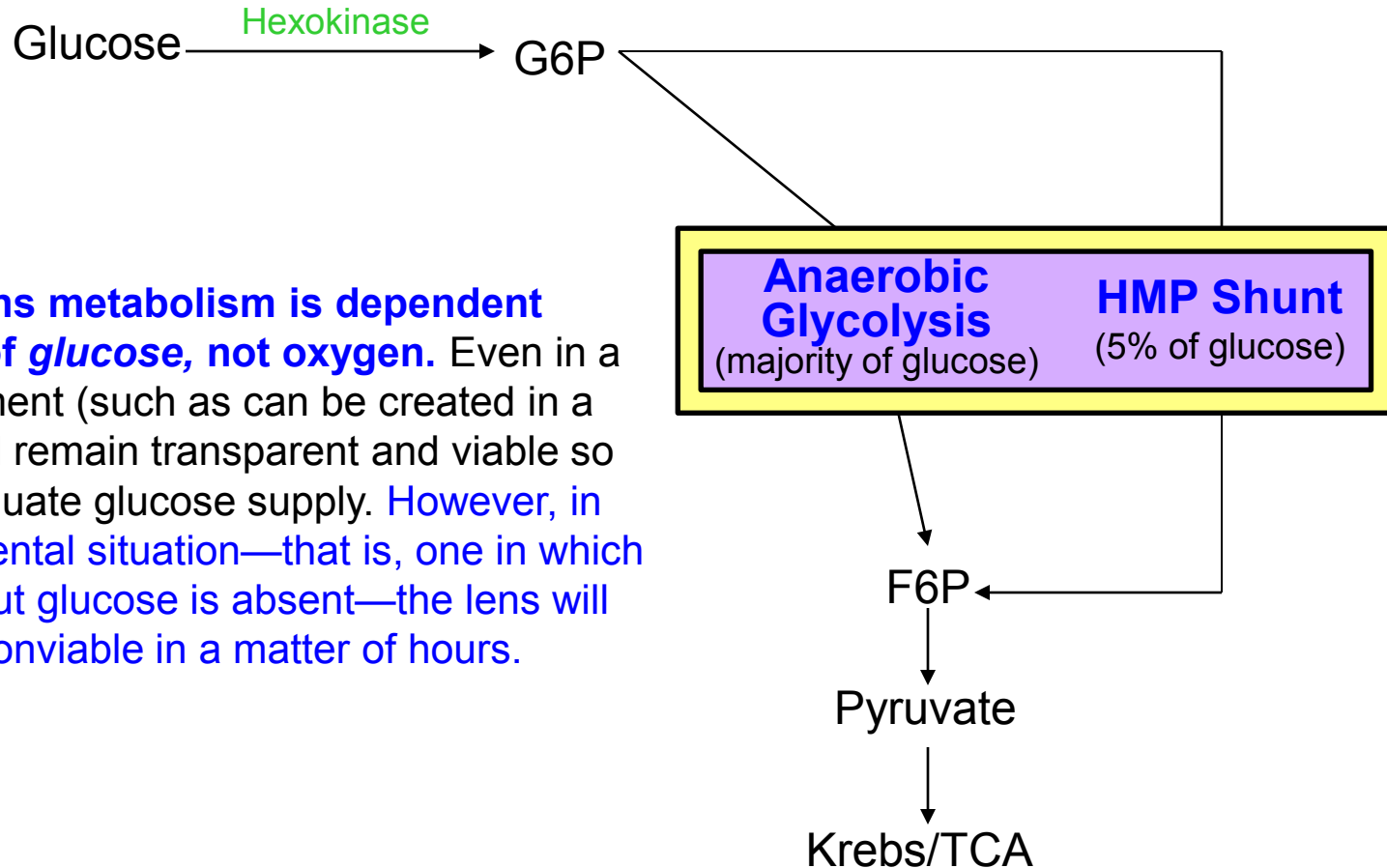
*The glycolytic nature of lens metabolism is the reason a particular organic ion is present in aqueous humor. Which ion?*



The top-line point: **Lens metabolism is dependent upon the presence of *glucose*, not *oxygen*.** Even in a zero-oxygen environment (such as can be created in a lab setting), a lens will remain transparent and viable so long as it has an adequate glucose supply. **However, in the reverse environmental situation—that is, one in which oxygen is abundant but glucose is absent—the lens will become cloudy and nonviable in a matter of hours.**

## Lens Metabolism

*The glycolytic nature of lens metabolism is the reason a particular organic ion is present in aqueous humor. Which ion?  
Lactate*



The top-line point: **Lens metabolism is dependent upon the presence of glucose, not oxygen.** Even in a zero-oxygen environment (such as can be created in a lab setting), a lens will remain transparent and viable so long as it has an adequate glucose supply. **However, in the reverse environmental situation—that is, one in which oxygen is abundant but glucose is absent—the lens will become cloudy and nonviable in a matter of hours.**

# Lens Metabolism

*The glycolytic nature of lens metabolism is the reason a particular organic ion is present in aqueous humor. Which ion?*  
**Lactate**—in fact, its aqueous concentration is higher than that in plasma

occasionally?  
usually?  
always?

Glucose  $\xrightarrow{\text{Hexokinase}}$  G6P

<b>Anaerobic Glycolysis</b> (majority of glucose)	<b>HMP Shunt</b> (5% of glucose)
--	-------------------------------------

F6P

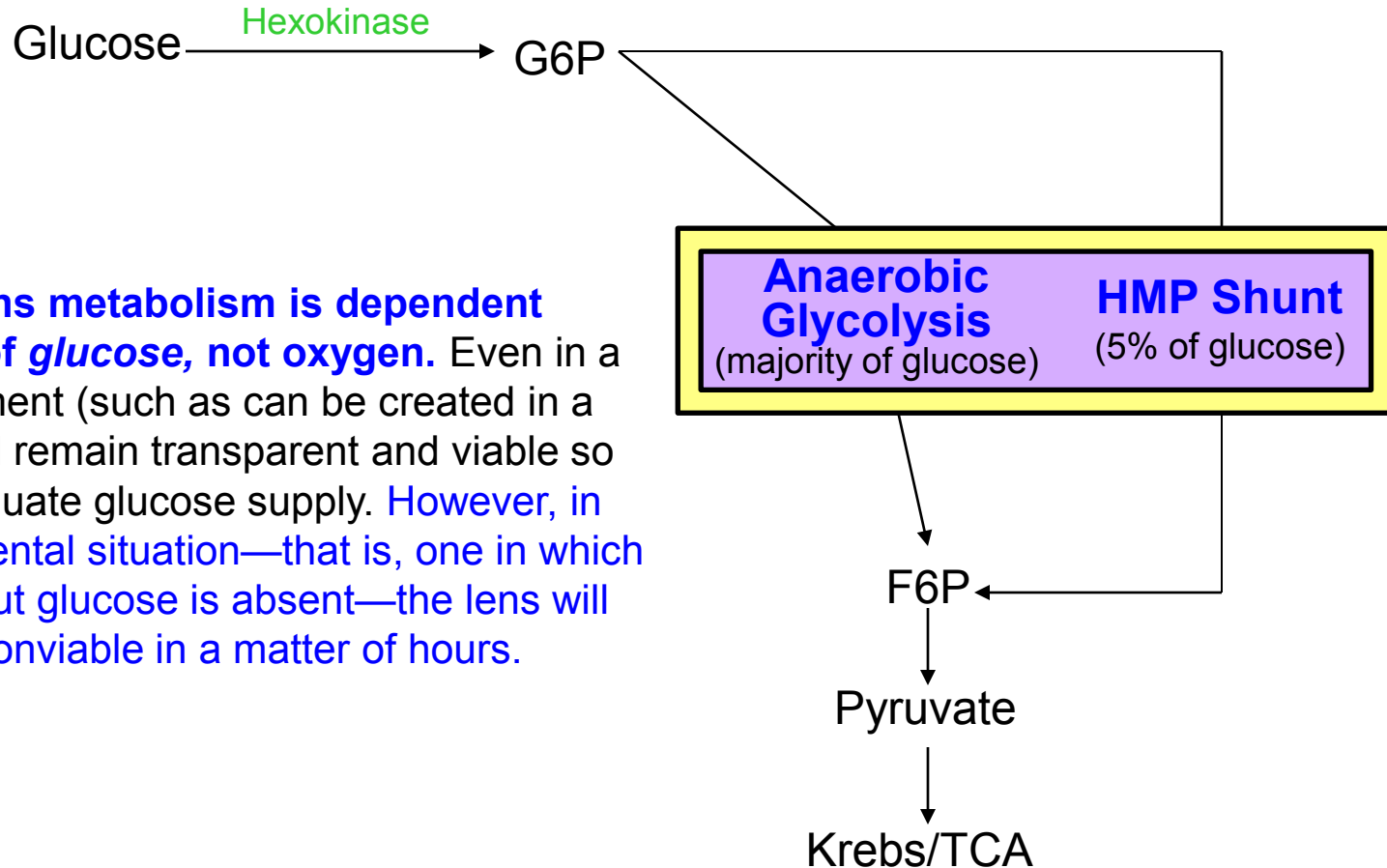
Pyruvate

Krebs/TCA

The top-line point: **Lens metabolism is dependent upon the presence of glucose, not oxygen.** Even in a zero-oxygen environment (such as can be created in a lab setting), a lens will remain transparent and viable so long as it has an adequate glucose supply. **However, in the reverse environmental situation—that is, one in which oxygen is abundant but glucose is absent—the lens will become cloudy and nonviable in a matter of hours.**

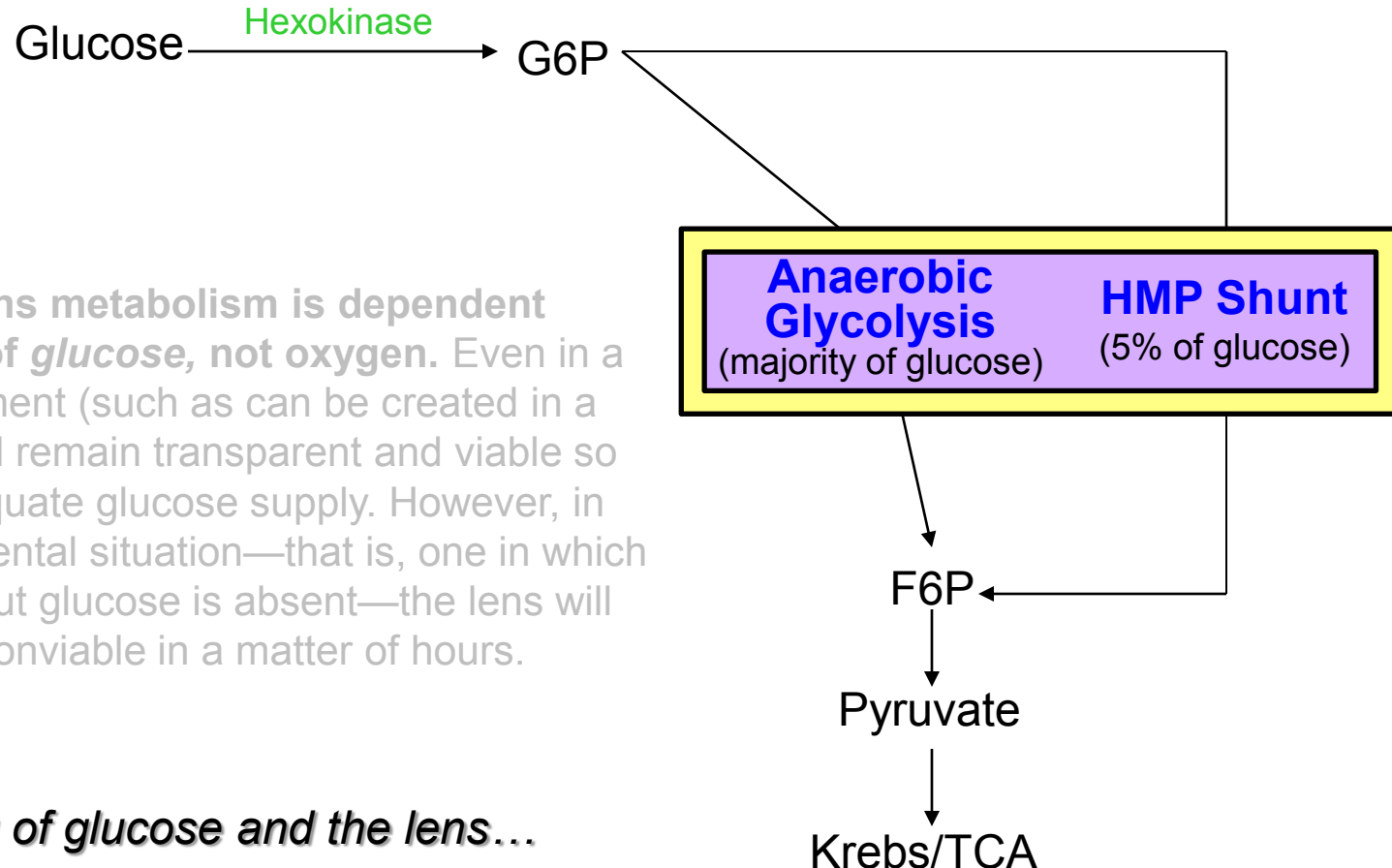
## Lens Metabolism

*The glycolytic nature of lens metabolism is the reason a particular organic ion is present in aqueous humor. Which ion? Lactate—in fact, its aqueous concentration is **always** higher than that in plasma*



The top-line point: **Lens metabolism is dependent upon the presence of glucose, not oxygen.** Even in a zero-oxygen environment (such as can be created in a lab setting), a lens will remain transparent and viable so long as it has an adequate glucose supply. **However, in the reverse environmental situation—that is, one in which oxygen is abundant but glucose is absent—the lens will become cloudy and nonviable in a matter of hours.**

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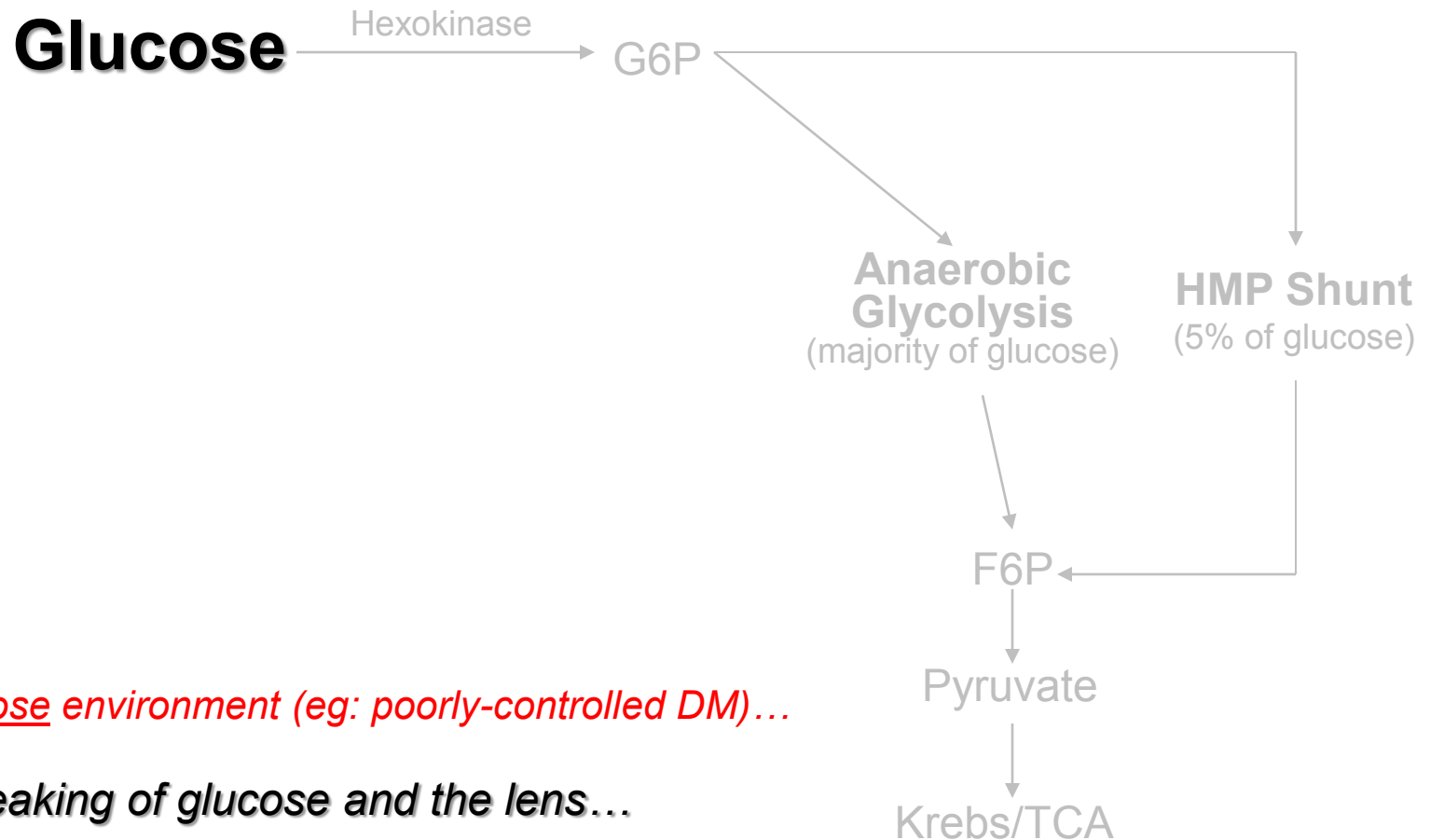
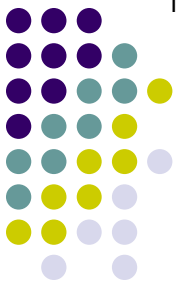
*Speaking of glucose and the lens...*

*No question yet—proceed when ready*



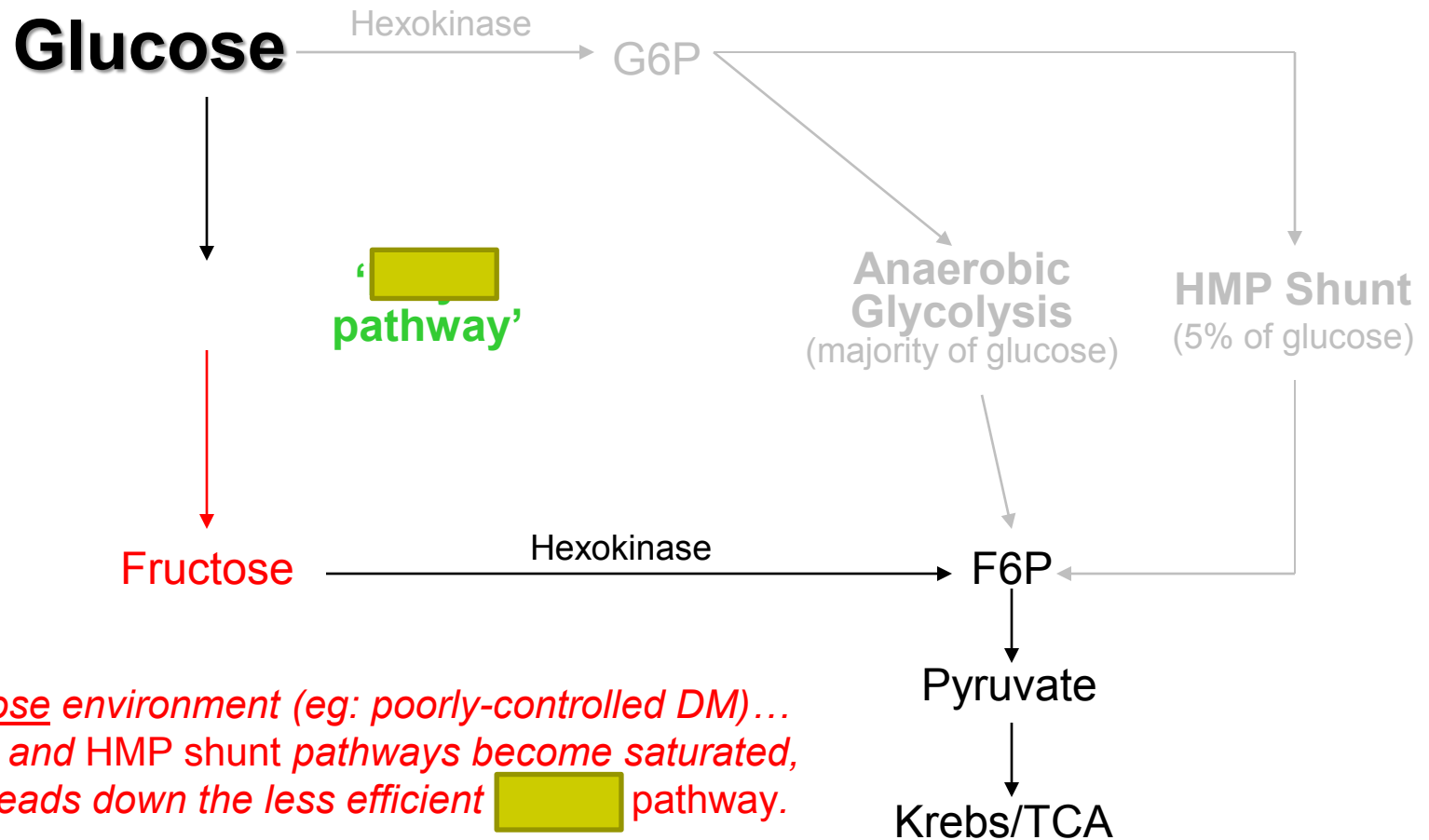
# Lens Metabolism

17



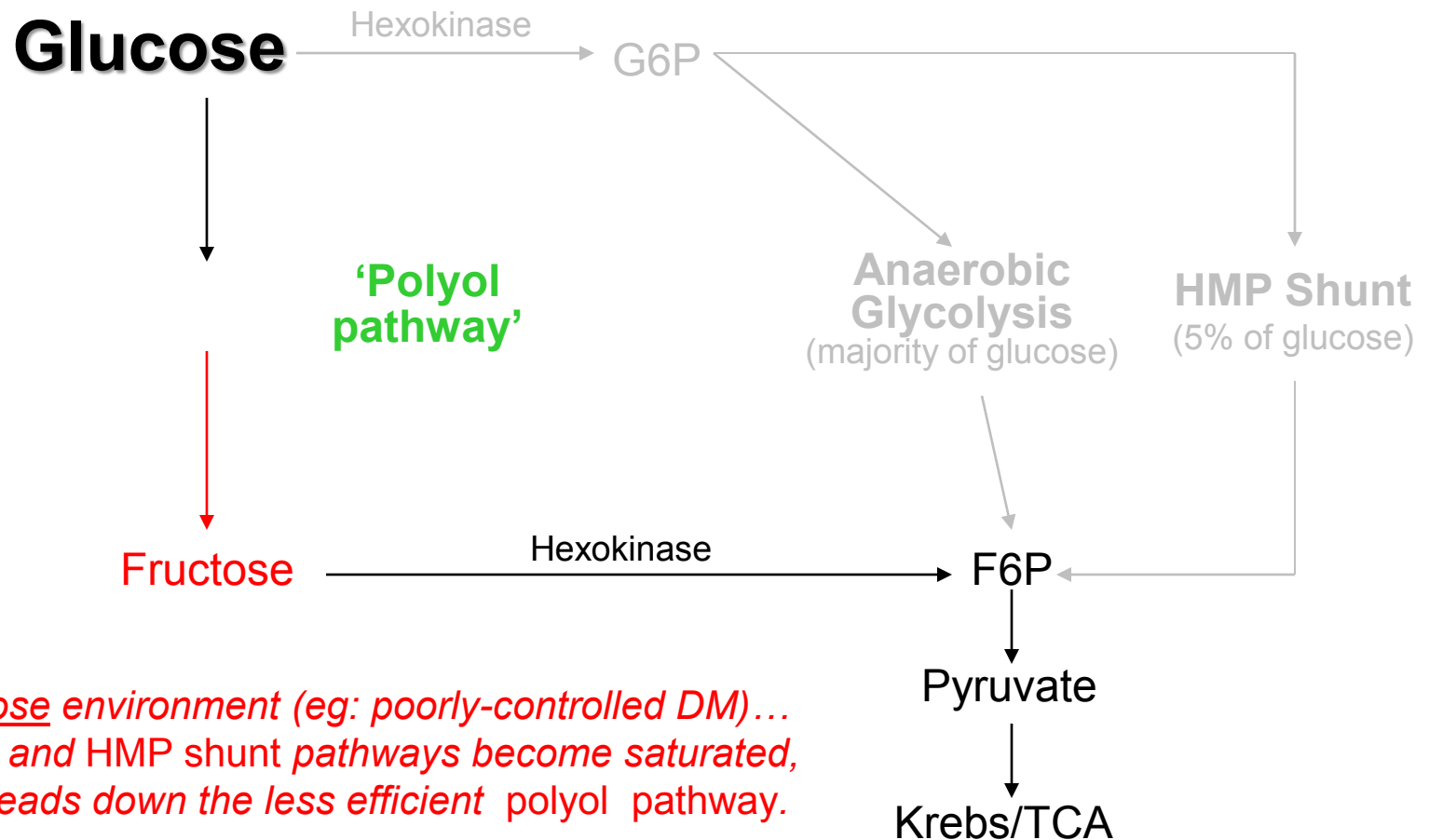
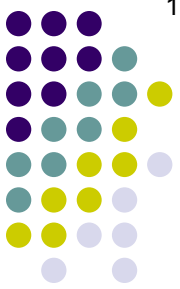
No question yet—proceed when ready

# Lens Metabolism

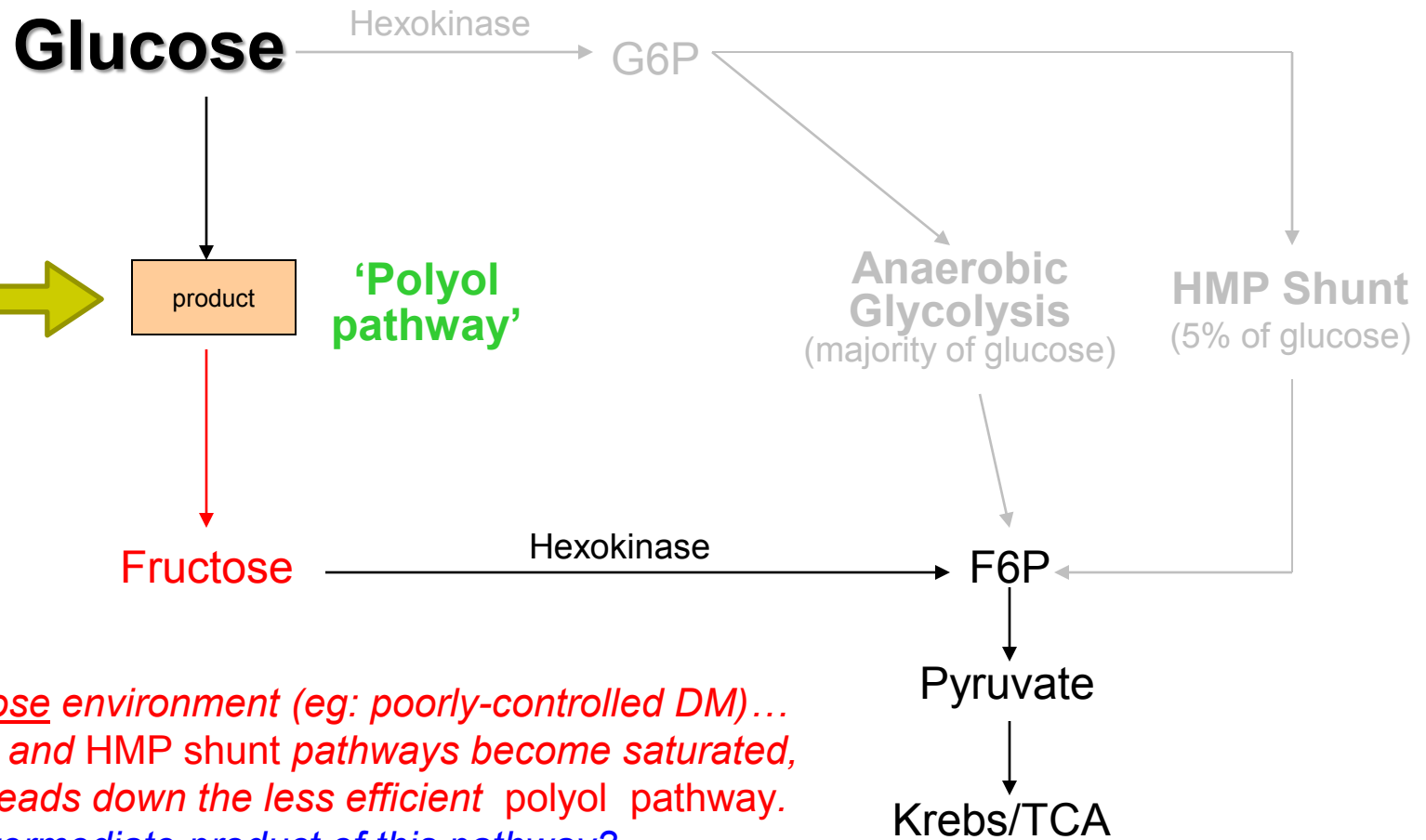
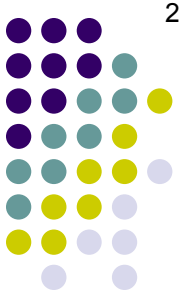


*In a high-glucose environment (eg: poorly-controlled DM)...  
The glycolysis and HMP shunt pathways become saturated,  
and glucose heads down the less efficient [ ] pathway.*

# Lens Metabolism

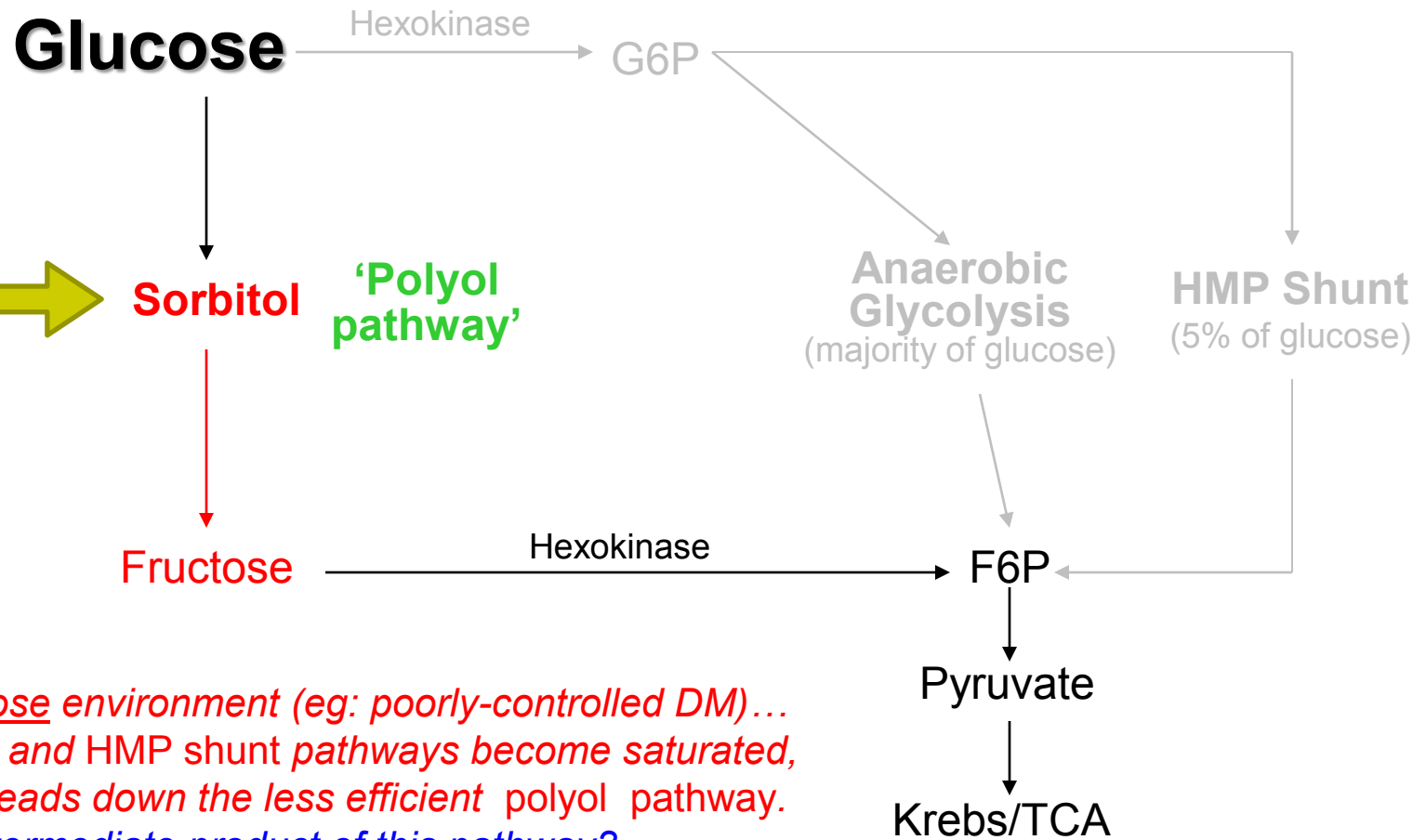


# Lens Metabolism



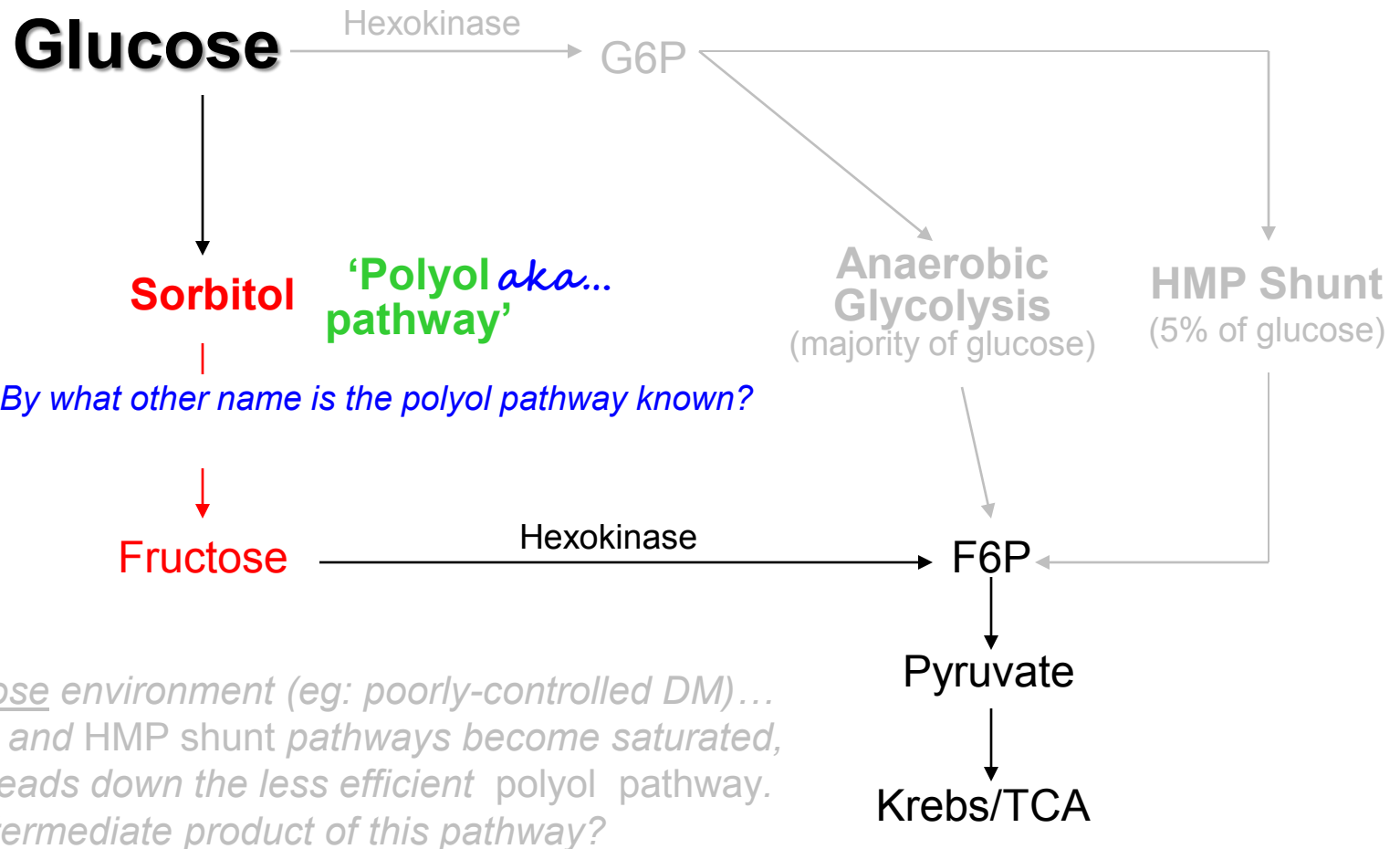
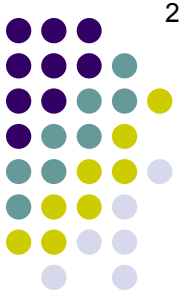
*In a high-glucose environment (eg: poorly-controlled DM)...  
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What is the intermediate product of this pathway?*

# Lens Metabolism

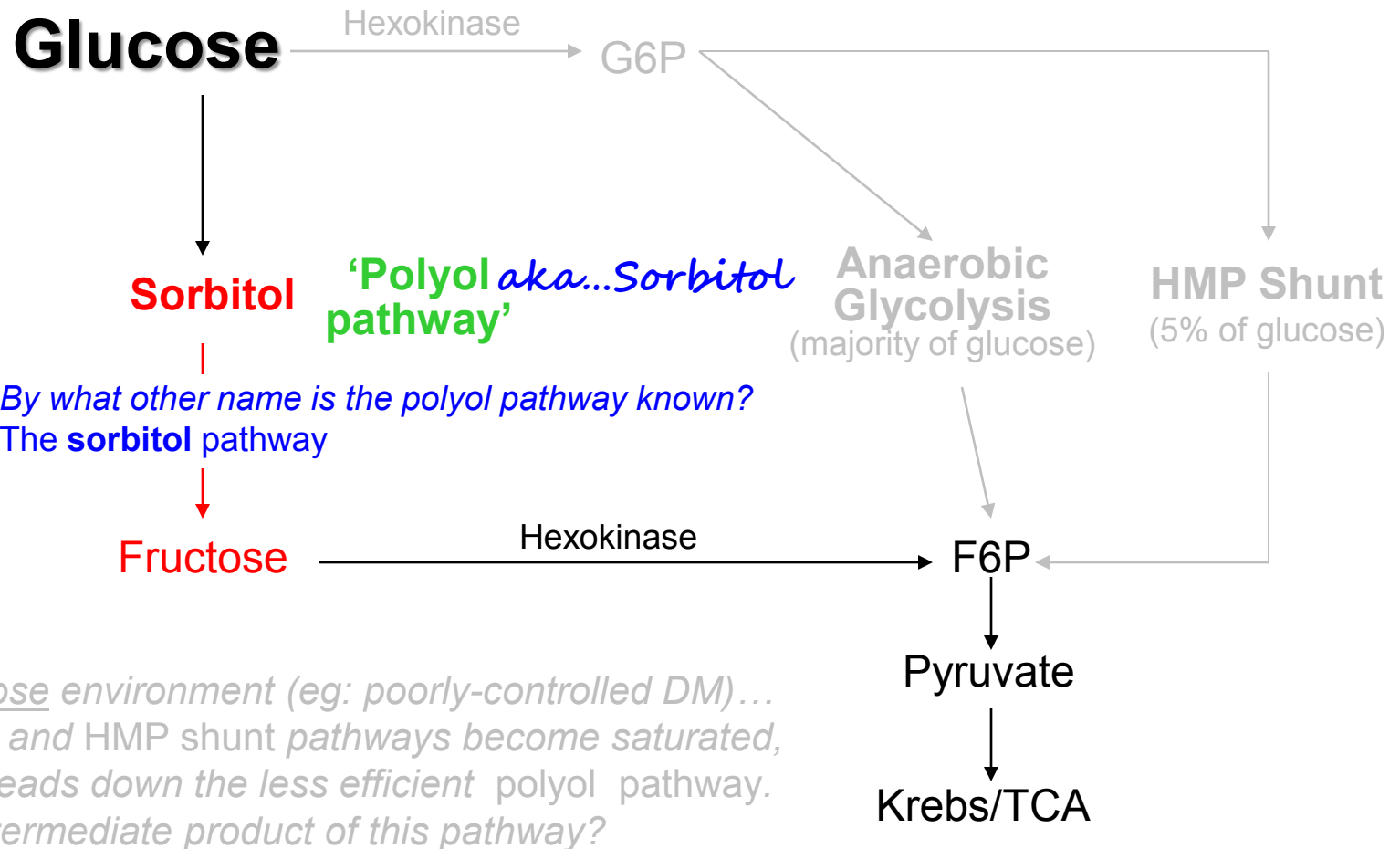
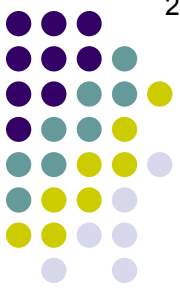


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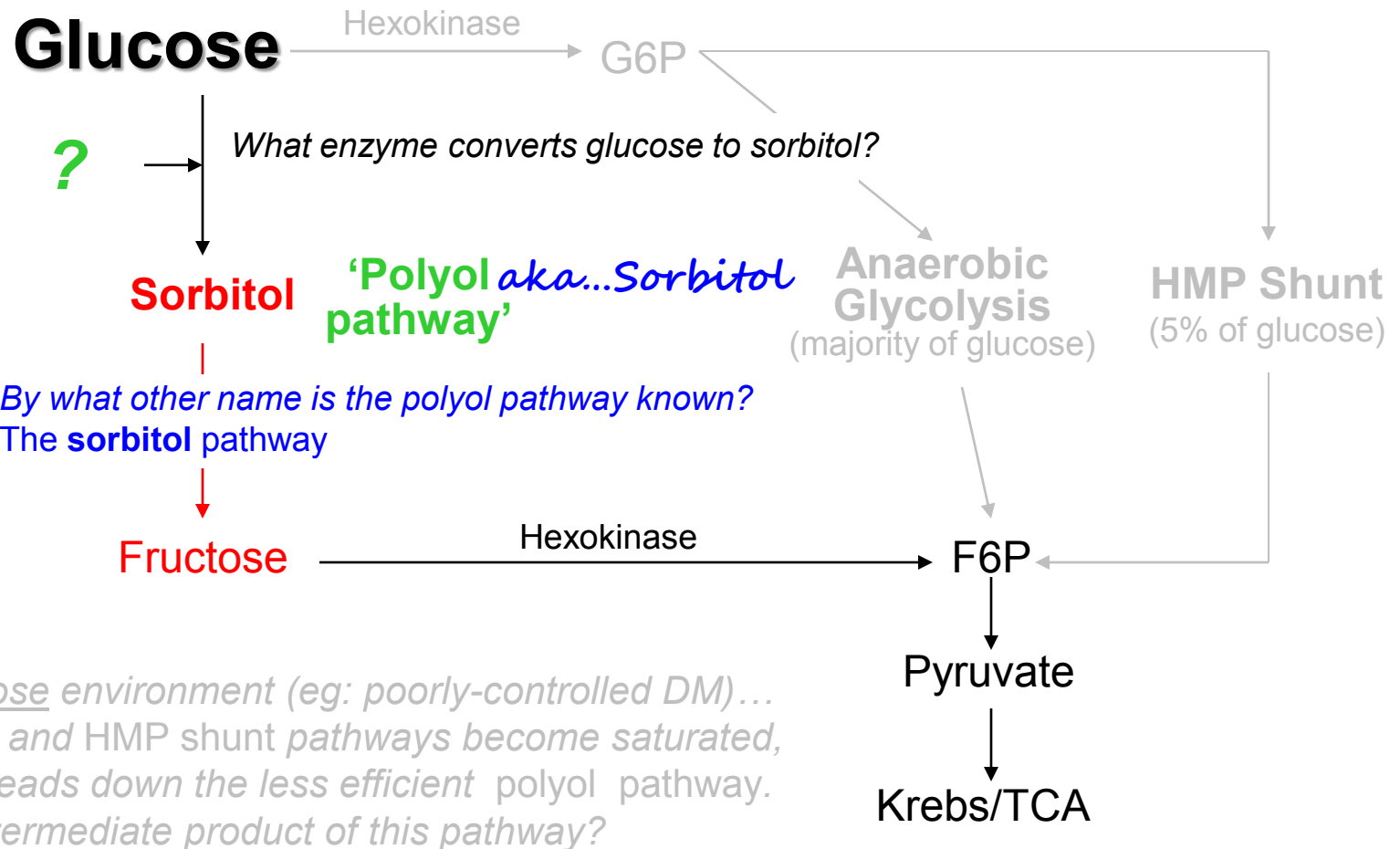
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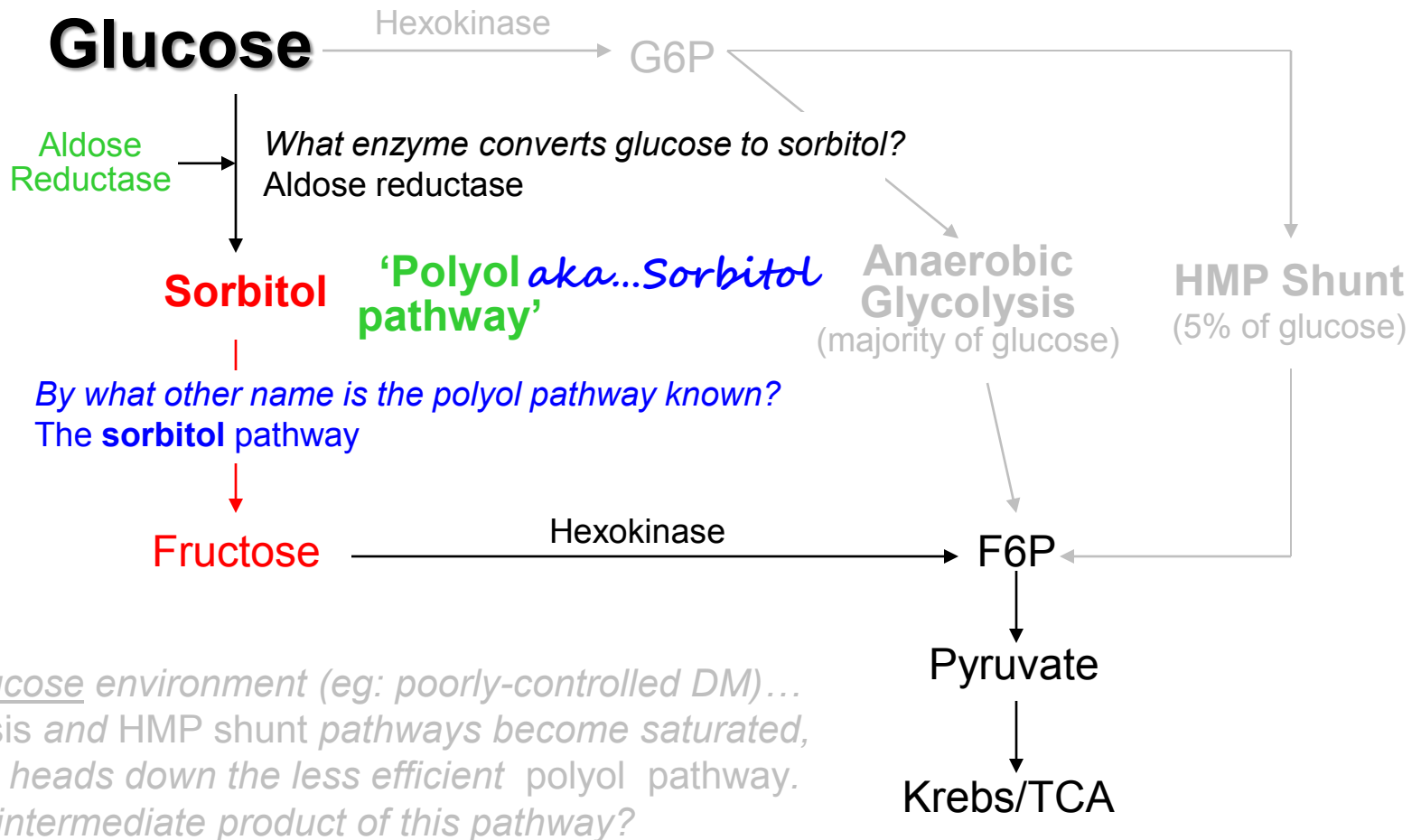


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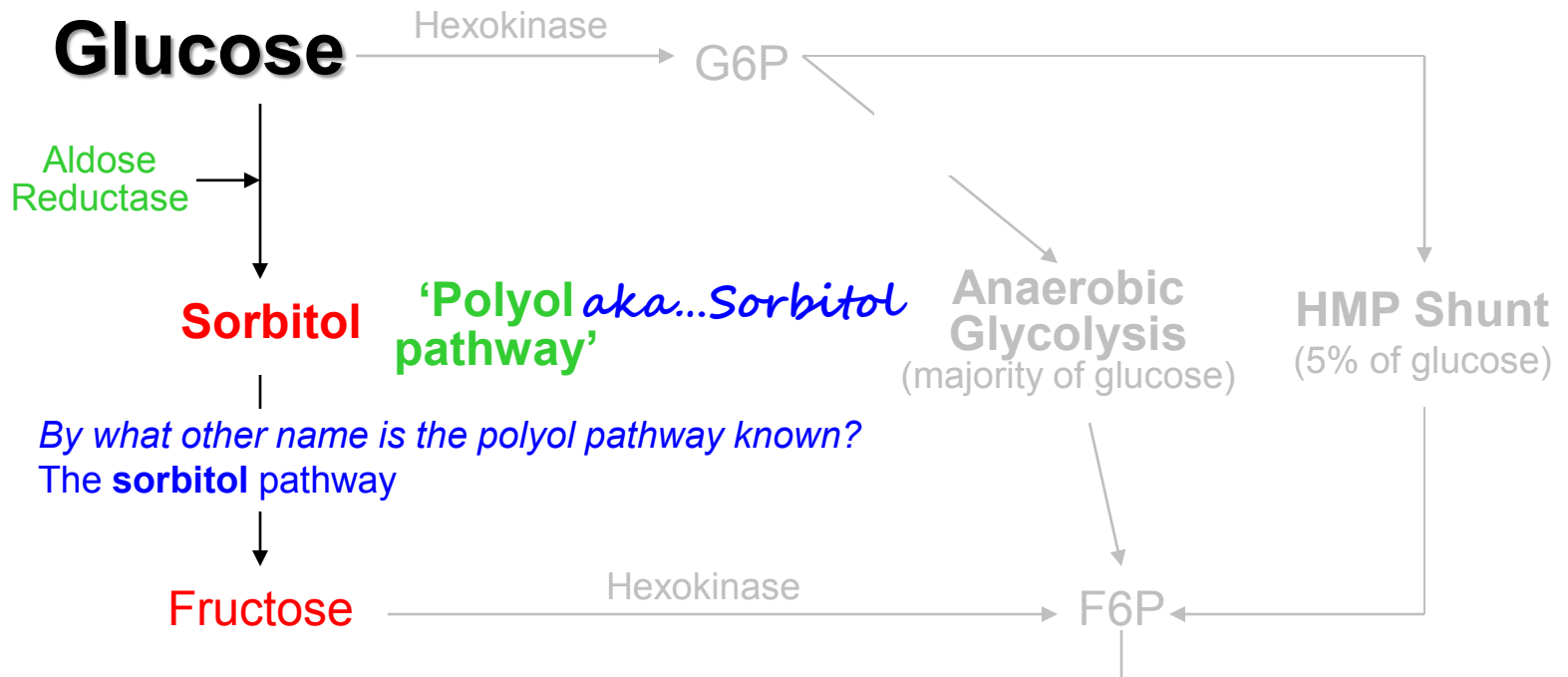
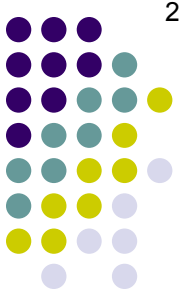




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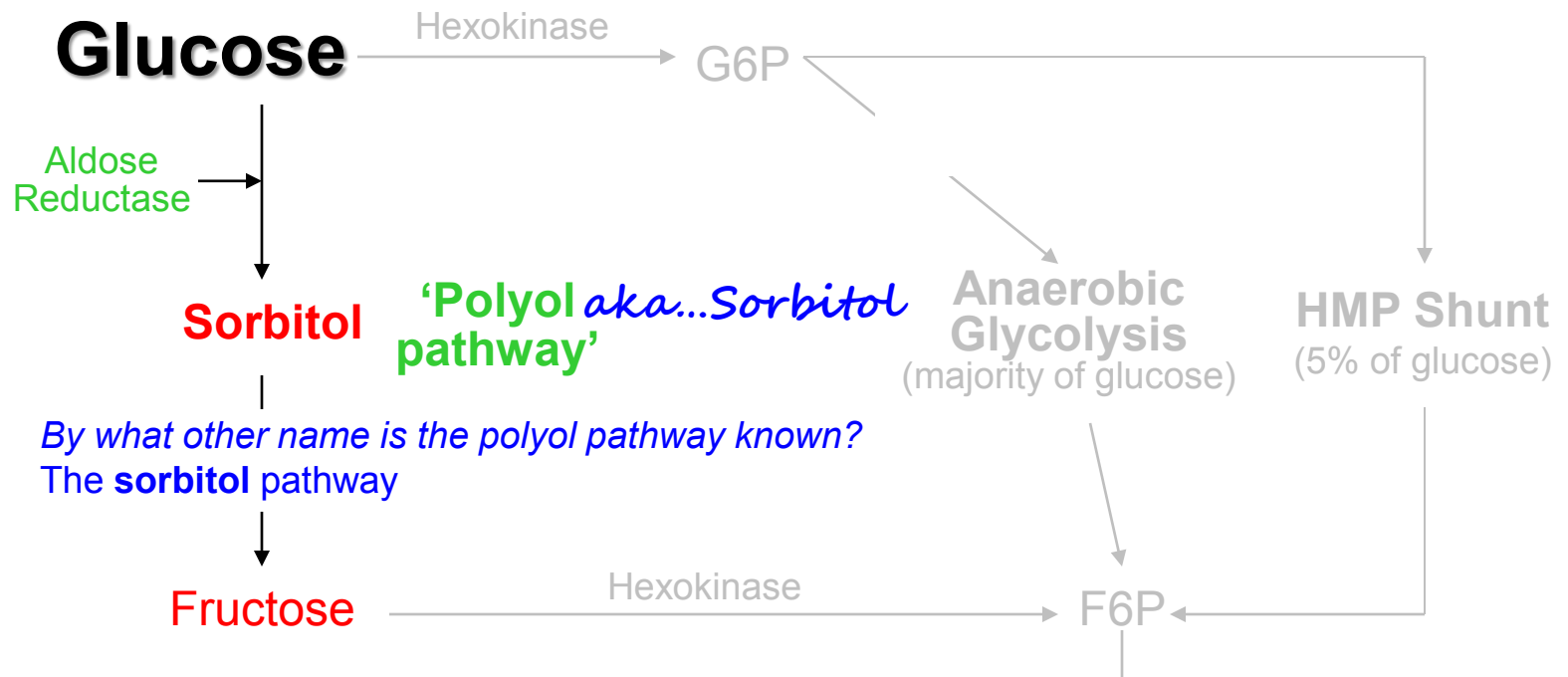


# Lens Metabolism



*What role does sorbitol play in the development of diabetic cataracts?*

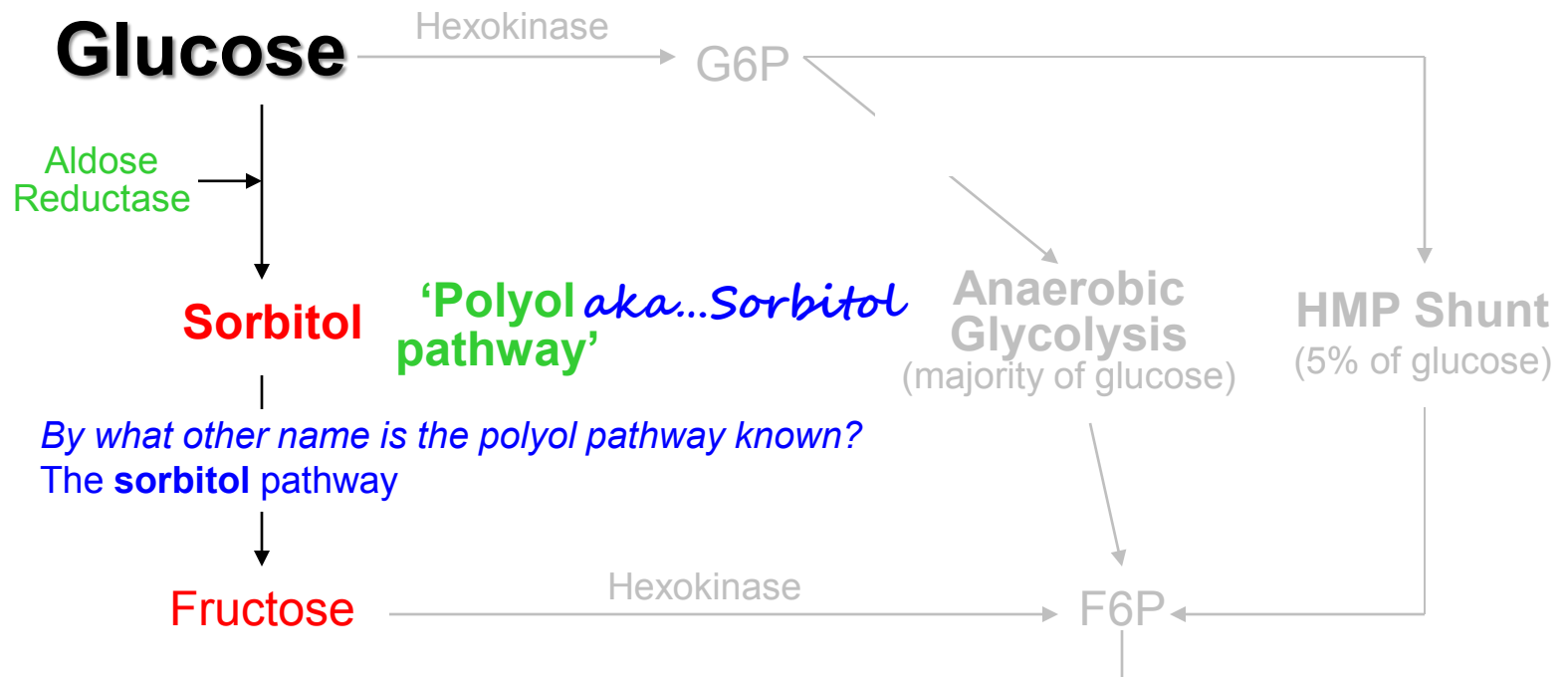
# Lens Metabolism



*What role does sorbitol play in the development of diabetic cataracts?*

A very central one. The conversion of sorbitol to fructose is slow and inefficient, the result being the accumulation of sorbitol within lens epithelial cells. This accumulation produces an osmotic gradient across the lens capsule, resulting in an influx of water into the lens and its cells.

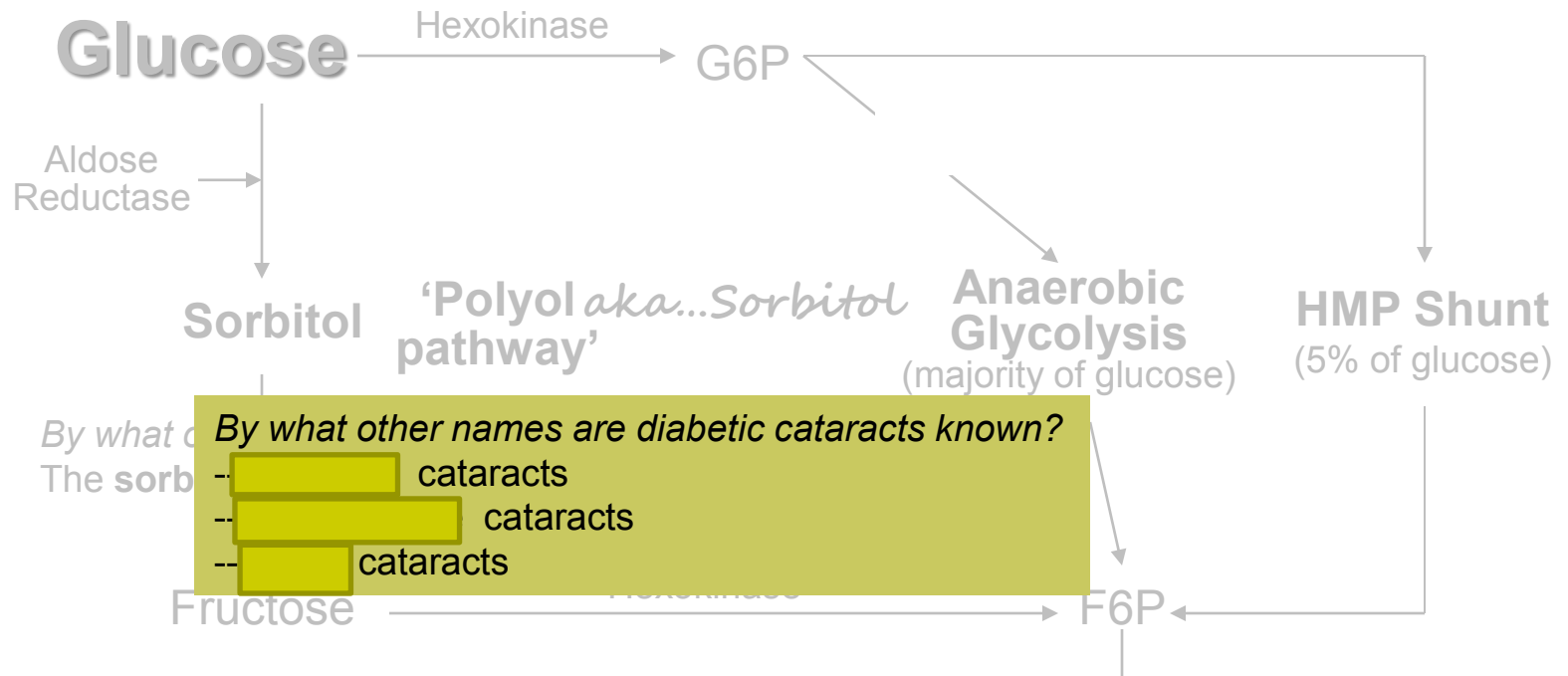
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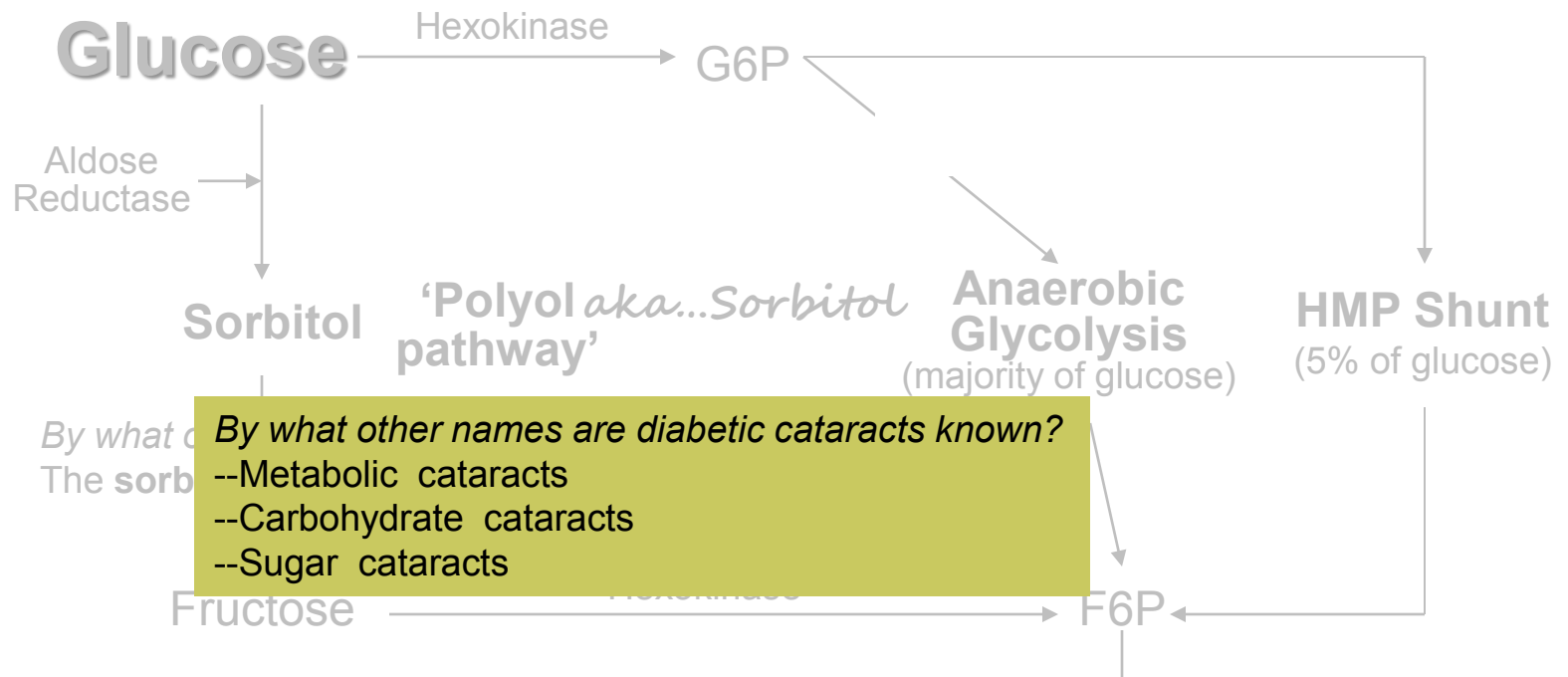
# Lens Metabolism



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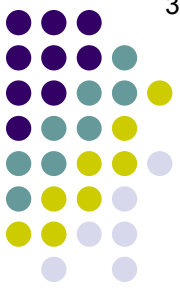
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# Lens Metabolism



*All diabetic cataracts are sugar cataracts, but not all sugar cataracts are diabetic cataracts.*

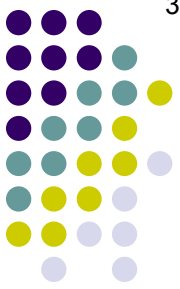
*(No question yet—proceed when ready)*



*What role does sorbitol play in the development of **diabetic cataracts**?*

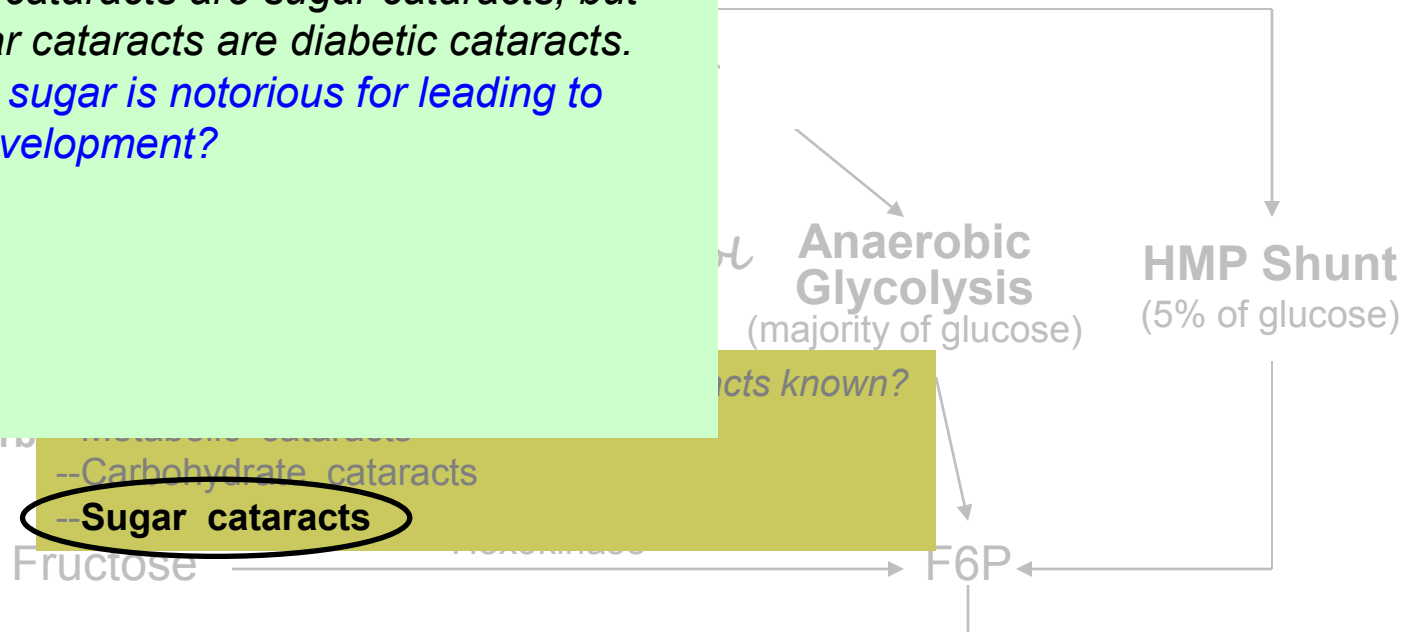
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# Lens Metabolism



?

All diabetic cataracts are sugar cataracts, but not all sugar cataracts are diabetic cataracts. What other sugar is notorious for leading to cataract development?



What role does sorbitol play in the development of **diabetic cataracts**?

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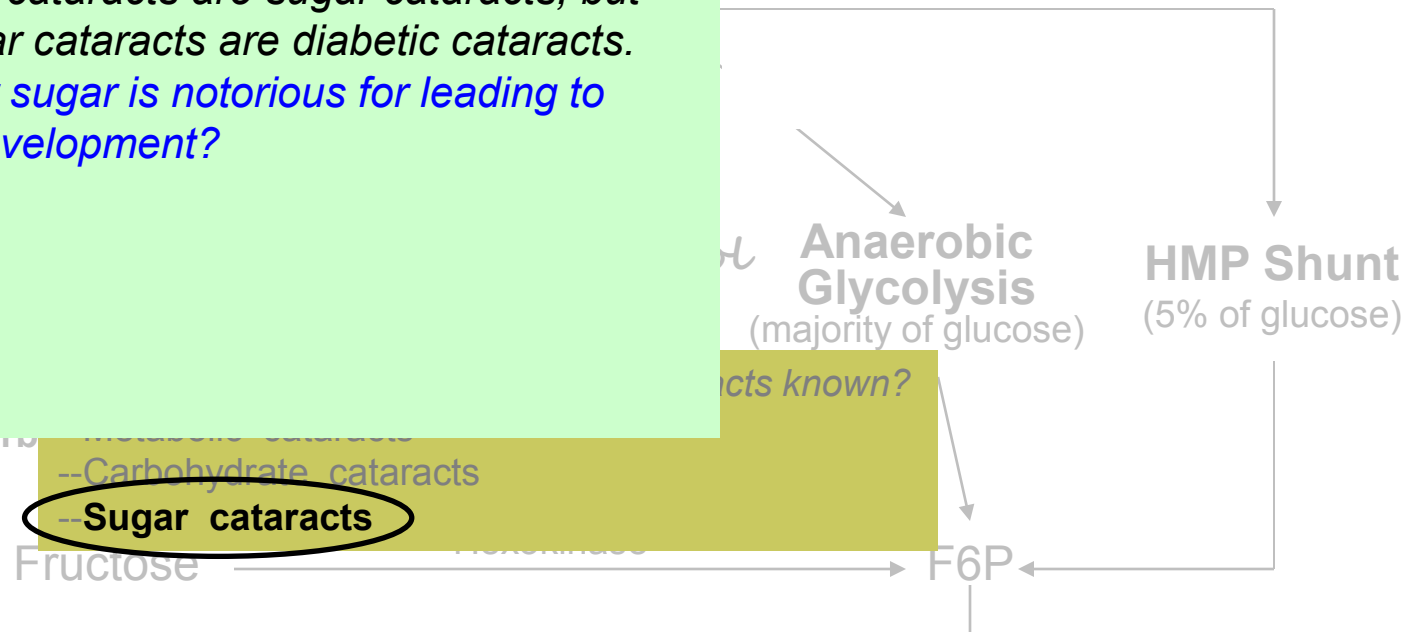


# Lens Metabolism



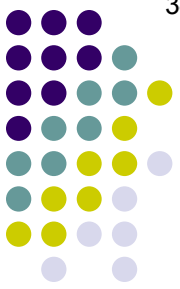
## Galactose

*All diabetic cataracts are sugar cataracts, but not all sugar cataracts are diabetic cataracts.*  
*What other sugar is notorious for leading to cataract development?*  
 Galactose



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## Lens Metabolism

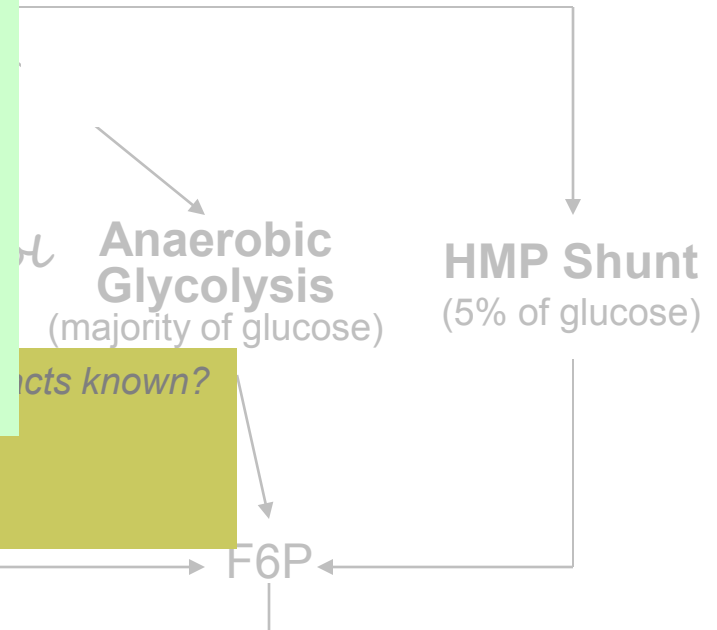
### Galactose (in ? )

*All diabetic cataracts are sugar cataracts, but not all sugar cataracts are diabetic cataracts.*

*What other sugar is notorious for leading to cataract development?*

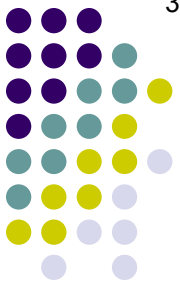
Galactose

*What is the name of the condition in which galactose leads to cataract development?*



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## Lens Metabolism

### Galactose (in galactosemia)

*All diabetic cataracts are sugar cataracts, but not all sugar cataracts are diabetic cataracts.*

*What other sugar is notorious for leading to cataract development?*

Galactose

*What is the name of the condition in which galactose leads to cataract development?*

**Galactosemia**

Fructose

Carbohydrate cataracts

**Sugar cataracts**

Anaerobic Glycolysis  
(majority of glucose)

HMP Shunt  
(5% of glucose)

acts known?

F6P

*What role does sorbitol play in the development of **diabetic cataracts**?*

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## Lens Metabolism



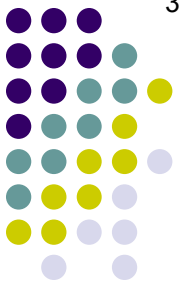
### Galactose (in *galactosemia*)

*Does the cataract in galactosemia stem from high galactose levels a la the way a diabetic cataract results from high glucose levels?*

MP Shunt  
(% of glucose)

Krebs/TCA

## Lens Metabolism



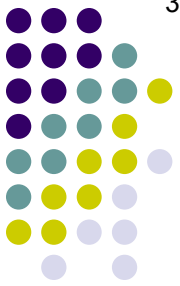
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Indeed it does

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## Lens Metabolism



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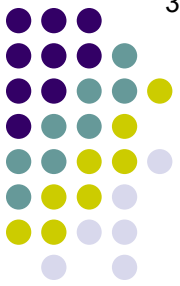
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*Is the cataract in galactosemia the result of the accumulation of a metabolic byproduct a la the accumulation of sorbitol in diabetic cataracts?*

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## Lens Metabolism



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## Lens Metabolism



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Indeed it is

*What is the metabolic byproduct that accumulates in galactosemia?*

MP Shunt  
(% of glucose)

Krebs/TCA

?



## Lens Metabolism



### Galactose (in galactosemia)

*Does the cataract in galactosemia stem from high galactose levels a la the way a diabetic cataract results from high glucose levels?*

Indeed it does

*Is the cataract in galactosemia the result of the accumulation of a metabolic byproduct a la the accumulation of sorbitol in diabetic cataracts?*

Indeed it is

*What is the metabolic byproduct that accumulates in galactosemia?*

Galactitol

MP Shunt  
(% of glucose)

Galactitol

Krebs/TCA

## Lens Metabolism



### Galactose (in galactosemia)

*Does the cataract in galactosemia stem from high galactose levels a la the way a diabetic cataract results from high glucose levels?*

Indeed it does

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Galactitol

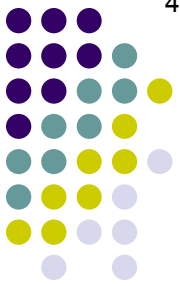
*What enzyme converts galactose to galactitol?*

MP Shunt  
(% of glucose)

Galactitol

Krebs/TCA

## Lens Metabolism



### Galactose (in galactosemia)

*Does the cataract in galactosemia stem from high galactose levels a la the way a diabetic cataract results from high glucose levels?*

Indeed it does

**Aldose  
Reductase**

*Is the cataract in galactosemia the result of the accumulation of a metabolic byproduct a la the accumulation of sorbitol in diabetic cataracts?*

Indeed it is

*What is the metabolic byproduct that accumulates in galactosemia?*

Galactitol

*What enzyme converts galactose to galactitol?*

Aldose reductase (yes, the same enzyme involved in diabetic cataracts)

MP Shunt  
(% of glucose)

**Galactitol**

Krebs/TCA



## Lens Metabolism

### Galactose (in galactosemia)

*Does the cataract in galactosemia stem from high galactose levels a la the way a diabetic cataract results from high glucose levels?  
Indeed it does*

**Aldose  
Reductase**

*Is the cataract in galactosemia the result of the accumulation of a metabolic*

*The fact that aldose reductase is the enzyme, does that mean the conversion of galactose to galactitol constitutes another example of the polyol pathway?*

**MP Shunt**  
(% of glucose)

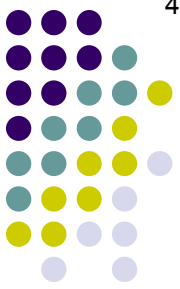
*What enzyme converts galactose to galactitol?  
Aldose reductase (yes, the same enzyme involved in diabetic cataracts)*

**Aldose reductase**

*Polyol  
pathway?*

**Galactitol**

Krebs/TCA



## Lens Metabolism

### Galactose (in galactosemia)

Does the cataract in galactosemia stem from high galactose levels a la the way a diabetic cataract results from high glucose levels?  
Indeed it does

**Aldose  
Reductase**

Is the cataract in galactosemia the result of the accumulation of a metabolic

The fact that aldose reductase is the enzyme, does that mean the conversion of galactose to galactitol constitutes another example of the polyol pathway?  
It does indeed

What enzyme converts galactose to galactitol?

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Yes, the same enzyme involved in diabetic cataracts)

Polyol  
pathway!

MP Shunt  
(% of glucose)

**Galactitol**

Krebs/TCA



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It does indeed. For both galactose and glucose, aldose reductase reduces the sugar to its corresponding two words (galactitol and sorbitol, respectively).

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Yes, the same enzyme involved in diabetic cataracts)

*Polyol  
pathway!*

**Galactitol**

Krebs/TCA

**MP Shunt**  
(% of glucose)



## Lens Metabolism

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**It does indeed.** For both galactose and glucose, aldose reductase reduces the sugar to its corresponding sugar alcohol (galactitol and sorbitol, respectively).

*What enzyme converts galactose to galactitol?*

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**Galactitol**

Krebs/TCA

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# Lens Metabolism



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**MP Shunt**  
(% of glucose)

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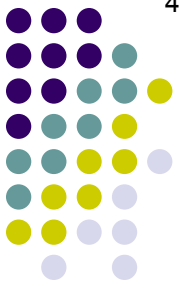
*(Recalling the organic-chemistry naming convention for alcohols should help you hang on to this factoid)*

*Polyol  
pathway!*

**Galactitol**

Krebs/TCA





## Lens Metabolism

### Galactose (in galactosemia)

*Does the cataract in galactosemia stem from high galactose levels a la the way a diabetic cataract results from high glucose levels?*

Indeed it does

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Reductase**

*Is the cataract in galactosemia the result of the accumulation of a metabolic byproduct a la the accumulation of sorbitol in diabetic cataracts?*

Indeed it is

*What is the metabolic byproduct that accumulates in galactosemia?*

Galactitol

*What enzyme converts galactose to galactitol?*

Aldose reductase (yes, the same enzyme involved in diabetic cataracts)

*How does galactitol get into the Krebs cycle?*

**MP Shunt**  
(% of glucose)

**Polyol  
pathway**

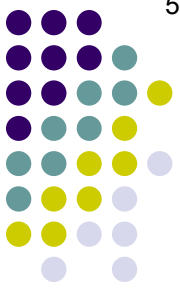
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**?**

**Krebs/TCA**



# Lens Metabolism



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It doesn't—it is metabolically inert, and simply accumulates

*Polyol  
pathway*

**MP Shunt**  
(% of glucose)

**Galactitol**



Krebs/TCA

## Galactose (in *galactosemia*)

Indeed it does

*Polyol pathway*

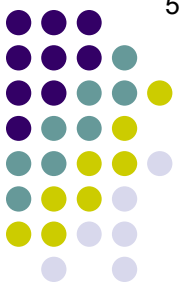
Indeed it is

**MP Shunt**  
(% of glucose)

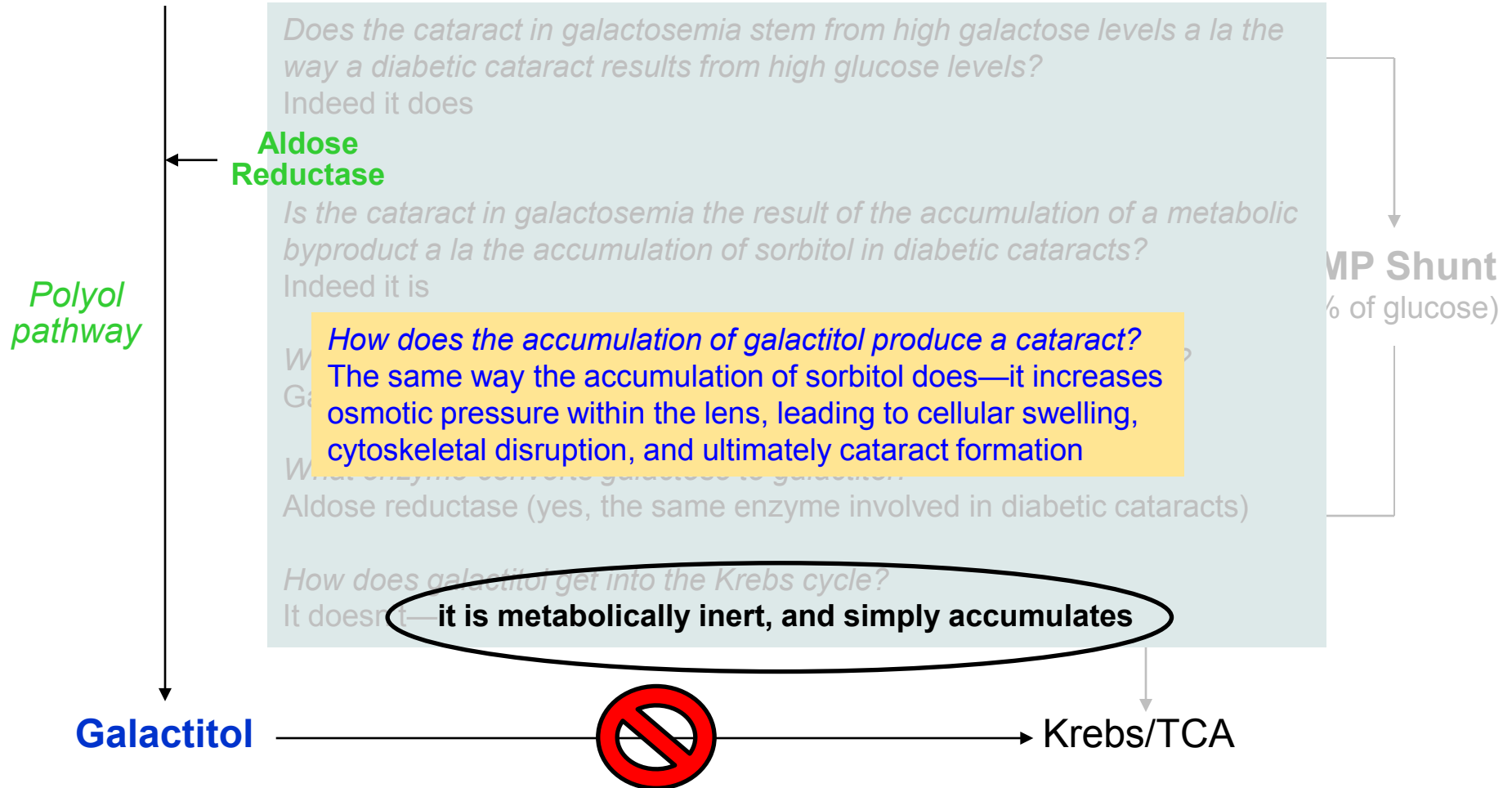
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## ► Krebs/TCA

# Lens Metabolism



## Galactose (in galactosemia)



# Lens Metabolism



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Reductase**

*Is the cataract in galactosemia the result of the accumulation of a metabolic*

Pol  
path

**For more on diabetic cataracts, see slide-set L14**  
**For more on galactosemia, see set P16**

*osmotic pressure within the lens, leading to cellular swelling, cytoskeletal disruption, and ultimately cataract formation*

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It doesn't—it is metabolically inert, and simply accumulates

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Krebs/TCA